Vascular Compliance in Women Post Gestational Diabetes with Impaired Glucose Tolerance and Normal Glucose Tolerance

by

Cheryl Caul

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Nursing

Edmonton, Alberta

Spring, 2007

Library and Archives Canada

Published Heritage Branch

395 Wellington Street
Ottawa ON K1A 0N4
Canada

Bibliothèque et Archives Canada

Direction du Patrimoine de l'édition

395, rue Wellington
Ottawa ON K1A 0N4
Canada

Your file Votre référence
ISBN: 978-0-494-29913-5
Our file Notre référence
ISBN: 978-0-494-29913-5

NOTICE:
The author has granted a non-exclusive license allowing Library and Archives Canada to reproduce, publish, archive, preserve, conserve, communicate to the public by telecommunication or on the Internet, loan, distribute and sell theses worldwide, for commercial or non-commercial purposes, in microform, paper, electronic and/or any other formats.

The author retains copyright ownership and moral rights in this thesis. Neither the thesis nor substantial extracts from it may be printed or otherwise reproduced without the author's permission.

AVIS:
L'auteur a accordé une licence non exclusive permettant à la Bibliothèque et Archives Canada de reproduire, publier, archiver, sauvegarder, conserver, transmettre au public par télécommunication ou par l'Internet, prêter, distribuer et vendre des thèses partout dans le monde, à des fins commerciales ou autres, sur support microforme, papier, électronique et/ou autres formats.

L'auteur conserve la propriété du droit d'auteur et des droits moraux qui protège cette thèse. Ni la thèse ni des extraits substantiels de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation.

In compliance with the Canadian Privacy Act some supporting forms may have been removed from this thesis.

While these forms may be included in the document page count, their removal does not represent any loss of content from the thesis.

Conformément à la loi canadienne sur la protection de la vie privée, quelques formulaires secondaires ont été enlevés de cette thèse.

Bien que ces formulaires aient inclus dans la pagination, il n'y aura aucun contenu manquant.

Canada

Dedication

To my husband Andy for reminding me of what is important in life

&

To my Mom who always believed

&

To my brother Robert Eugene "Tuf" who passed away during my masters studies

&

To my friends, Connie and Marcie, without whose support this endeavor would never have been accomplished

Abstract

Diabetes mellitus is a primary cause of cardiovascular disease. Decreased vascular compliance correlates with hyperglycemia. Limited research exists on vascular compliance in women with gestational diabetes mellitus (GDM).The purpose of this study was to detect vascular changes in women with a recent history of GDM. A cross-sectional, comparative design was used to assess vascular compliance, blood pressure, and waist:hip ratio in women post GDM with impaired glucose tolerance (IGT) or normal glucose tolerance (NGT) with women who did not have GDM acting as a control group. HDI/PulseWave™ Cardiovascular Profiling Instrument CR-2000 was utilized for analysis and one way ANOVA tested for differences. Although there was no difference in vascular compliance among the three groups, waist:hip ratio was significantly different. Women with a history of GDM demonstrate significantly higher waist:hip ratio compared to the control group. Increased waist:hip ratio is a predictor of the development of type 2 diabetes and its major complication of cardiovascular disease (CVD). Lifestyle modification can prevent type 2 diabetes in adults with IGT; therefore nursing practice needs to focus on reducing this modifiable risk factor to reduce the burden of DM and incidence of CVD in this population.

Acknowledgements

I would like to offer my sincere gratitude to Dr. Constance Chik for her guidance and expertise in the development and successful completion of this study. Her encouragement, support, and sense of humor made this a remarkable learning experience. I would also like to thank Dr. Colleen Norris and Dr. Beverly Williams for their valuable assistance with the completion of this thesis. Finally, I am indebted to the many new Moms who welcomed me into their homes and graciously participated in this study.

Table of Contents

Chapter 1: Introduction.....1

Purpose of the Study.....2

Significance of the Study.....2

Chapter 2: Literature Review.....5

Vascular Compliance.....5

Vascular compliance with diabetes, impaired glucose tolerance, and impaired fasting glucose.....5

Gestational Diabetes.....7

Insulin resistance.....7

Prevalence.....8

Vascular compliance.....9

Measurement of Vascular Compliance.....11

Waveform Analysis.....11

Description.....11

Rationale for Use.....12

Limitations.....13

Summation.....14

Chapter 3: Research Method.....15

Design.....15

Sample.....15

Sampling Method.....16

Ethical Considerations.....18

Sample Size.....19
Data Collection.....20
Operational Definitions.....21
Data Analysis.....21
Chapter 4: Results.....23
Participant Characteristics.....23
Glucose Tolerance on Vascular Compliance, Blood Pressure, and Waist:Hip Ratio.....24
Chapter 5: Discussion.....37
Relationship of Waist:Hip Ratio to Glucose Tolerance and CVD.....37
Ethnicity and Vascular Compliance.....38
Vascular Compliance, Glucose Tolerance & Pregnancy.....39
Implications for Nursing Practice.....41
Strengths, Limitations, and Direction for Future Research.....43
Strengths.....44
Limitations.....44
Future Research.....45
Conclusion.....46
References.....49

Appendices.....59

Appendix A: Recruitment Poster.....60

Appendix B: Ethical approval.....61

Appendix C: Information Sheet.....62

Appendix D: Consent Form.....64

Appendix E: Questionnaire.....66

Appendix F: Inclusion Criteria and Exclusion Criteria.....69

List of Tables

Table 1 Participants Demographics and Clinical Characteristic.....25

Table 2 One Way ANOVA between the group with abnormal glucose tolerance and the combined group of normal glucose tolerance.....31

Table 3 One way ANOVA comparing Vascular Compliance and Blood Pressure in Caucasians and Non-Caucasian.....32

List of Figures

Figure 1.1 Screening for type 2 diabetes, IFG, and IGT.....3

Figure 2.1 Typical central aortic pressure waveform.....12

Figure 3.1 Sample of a HDI/PulseWave™CR-2000 Profile Report.....22

Figure 4.1 Graph of Differences of Large Artery Compliance between Groups.....26

Figure 4.2 Graph of Differences of Small Artery Compliance between Groups.....27

Figure 4.3 Graph of Differences of Systolic BP between Groups.....28

Figure 4.4 Graph of Differences of Diastolic BP between Groups.....29

Figure 4.5 Graph of Differences of Waist:Hip Ratio between Groups.....30

Figure 4.6 Differences of Small Artery Elasticity between Filipinos and Non-Filipinos.....33

Figure 4.7 Regression Analysis of Age to Large Artery Compliance.....35

Figure 4.8 Regression Analysis of Age to Small Artery Compliance.....36

CHAPTER 1

Introduction

Diabetes Mellitus (DM) is a metabolic disorder with defective insulin secretion, insulin action or both, and characterized by the presence of hyperglycemia. DM occurs in special populations, one of which is pregnant women, and is classified as Gestational Diabetes Mellitus (GDM). GDM is defined by Metzger & Coustan (1998) as, "carbohydrate intolerance of varying degrees of severity with onset or first recognition during pregnancy" (p. B162), which results in hyperglycemia.

It is recommended by the Canadian Diabetes Clinical Practice Guidelines (2003), that all women with a history of GDM have an oral glucose tolerance test (OGTT) to assess glucose tolerance within six months of delivery since all women with a history of GDM are at an increased risk for type 2 DM (Kim, Newton, & Knopp, 2002). Post delivery, a significant portion of the population with GDM will no longer experience carbohydrate intolerance and will return to normal glucose tolerance. However, this will not occur in all cases and some women will be diagnosed with either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) or both. IFG and IGT refer to abnormal blood sugars that are above normal glycemic levels, but are below the threshold for the diagnosis for DM (Figure 1.1).

It is well established that DM is a primary cause of cardiovascular disease (CVD) (Folsom et al., 1997; Kannal & McGee, 1979; Stamler, Vaccaro, Neaton, & Wentworth, 1993) and that cardiovascular mortality is related to the degree of hyperglycemia in individuals with diabetes (Moss, Klein, Klein, & Meuer, 1994). Non-diabetic degrees of hyperglycemia are also associated with cardiovascular events (Coutinho, Gerstein,

Wang, & Yusef, 1999). Of all complications of DM, CVD has the highest mortality and morbidity (Haffner, Lehto, Ronnemaa, Pyorala, & Laakso, 1998).

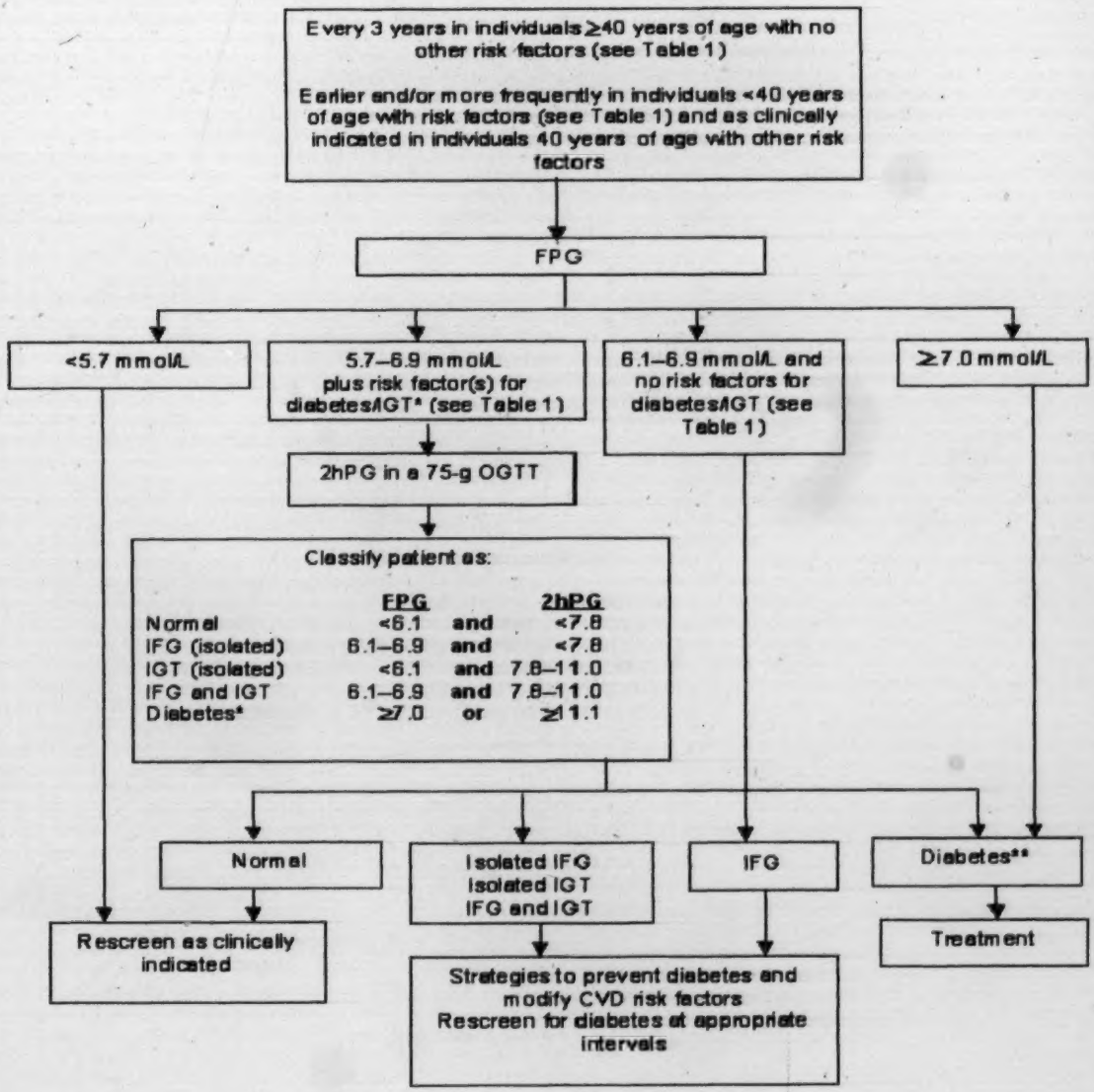
In recent years, vascular compliance has been researched in subjects with DM and IGT. "Deteriorating glucose tolerance is associated with increased central and peripheral arterial stiffness, which may partly explain why both DM-2 [diabetes mellitus-type 2] and IGM [impaired glucose metabolism] are associated with increased cardiovascular risk" (Schram et al., 2004, p. 176). Limited vascular research has been completed post GDM and a trend is emerging that reduced vascular compliance has developed post delivery.

Purpose of Study

The purpose of this nursing research is to detect change in vascular compliance in women with either IGT or IFG and normal glucose tolerance, with a recent history of GDM. The hypothesis of this research is that women with IGT or IFG, and normal glucose tolerance, who have had a recent pregnancy complicated by GDM, demonstrate decreased vascular compliance in large and small arteries as determined by non-invasive pulse wave analysis compared to controls with normal glucose metabolism during a recent pregnancy.

Significance of Study

Although individuals with type 1 DM, type 2 DM and IGT comprise the majority of the diabetes and glucose intolerant population, special diabetic populations, such as GDM, need to be researched. The main reason for the selection of this population is that this may represent a younger group of individuals who are at risk of cardiovascular disease.


Every 3 years in individuals ≥40 years of age with no other risk factors (see Table 1)
Earlier and/or more frequently in individuals <40 years of age with risk factors (see Table 1) and as clinically indicated in individuals 40 years of age with other risk factors
FPG
<5.7 mmol/L
5.7–6.9 mmol/L plus risk factor(s) for diabetes/IGT* (see Table 1)
6.1–6.9 mmol/L and no risk factors for diabetes/IGT (see Table 1)
≥7.0 mmol/L
2hPG in a 75-g OGTT
Classify patient as:
FPG 2hPG
Normal <6.1 and <7.8
IFG (isolated) 6.1–6.9 and <7.8
IGT (isolated) <6.1 and 7.8–11.0
IFG and IGT 6.1–6.9 and 7.8–11.0
Diabetes* ≥7.0 or ≥11.1
Normal
Isolated IFG
Isolated IGT
IFG and IGT
IFG
Diabetes**
Rescreen as clinically indicated
Strategies to prevent diabetes and modify CVD risk factors
Rescreen for diabetes at appropriate intervals
Treatment

FPG (fasting plasma glucose), 2hPG (2 hour plasma glucose)

Figure 1.1

Screening for type 2 diabetes, IFG, and IGT (Canadian Diabetes Association)

Nursing research needs not only to contribute to the body of nursing knowledge, but to also guide nursing practice. This is especially important given the expanding role of nurses in the Canadian health care system. "CNPI [Canadian Nurse Practitioner Initiative] envisioned a renewed health system that optimizes the contributions of nurse practitioners to the health of all Canadians. Nurse Practitioners will be recognized and utilized across Canada as essential providers of quality health care" (Canadian Nurses Association, 2007, para. 2). By establishing that women who have had a pregnancy complicated by GDM have decreased vascular compliance, the data generated can provide the foundation for nursing care to focus on the modifiable risk factors and treatment modalities to promote health and well being to reduce the incidence of both CVD mortality and morbidity of this specific diabetic population.

CHAPTER 2

Literature Review

Several different terms exist in the literature to characterize the cushioning function of an artery, such as distensibility, stiffness, elasticity, and compliance. All of these terms in relation to diabetes, IFG, and IGT were reviewed using the computer online search engines of Medline (1966-present) and GOOGLE to establish the correlation of decreased vascular compliance to increased glucose levels. The search then focused on GDM to provide an understanding of the relationship of insulin resistance to glucose intolerance, the prevalence of the disease, and vascular compliance in this specific diabetic population. Finally, measurement strategies (devices) used to determine vascular functioning was evaluated. Abstracts were reviewed for appropriateness of content from retrieved publications. If the content could contribute to the purpose of the thesis, the full publication was acquired through the library.

Vascular Compliance

Vascular compliance refers to the vascular elasticity and the storage of the vessels. It is the term chosen for this thesis due to its precise meaning. "Compliance is an absolute term, relating absolute diameter or volume change to change in pressure" (O'Rourke, 1995, p. 3).

Vascular compliance with diabetes, impaired glucose tolerance, and impaired fasting glucose

Vascular compliance has been researched extensively in humans with DM, IGT, and IFG, under a variety of conditions. The atherosclerosis risk in communities (ARIC) study completed by Salomaa, Riley, Kark, Nardo, and Folsom (1995) was the first to

identify "that persons with NIDDM or borderline glucose intolerance have stiffer arteries than their counterparts with normal glucose tolerance and that the decreased elasticity is independent of artery wall thickness" (p. 1432) in a population of 4701 subjects aged 45 to 64 years. This was consistent for the entire population of men, women, blacks, and whites, for several indices of common carotid artery stiffness, using non-invasive ultrasound methods. In addition, arterial stiffness was positively correlated with increasing concentrations of fasting glucose. Further research confirmed that vascular compliance was decreased in both type 1 DM and type 2 DM, IGT, and IFG (De Angelis et al., 2004; Emoto et al., 1998; Endemann et al., 2004; Henry et al., 2003; Romney & Lewanczuk, 2001; Schram et al., 2004; van dijk, Nijpels et al., 2000; Weinberger, Fineberg, & Feinbert, 2002).

The correlation of diminishing vascular compliance to increasing glucose levels has also been researched. Weinberger, Fineberg, and Fineberg, (2002) measured vascular compliance and glucose tolerance ($p < 0.001$) in both normotensive and hypertensive heterogeneous subjects with normal glucose tolerance, IGT, and DM. When the population of 275 was separated on the basis of glucose tolerance, Weinberger et al. (2002) concluded "vascular abnormalities begin with minor, no diabetic impairment of carbohydrate tolerance, rather than only occurring after the manifestation of diabetes and that they are independent of age" (p. 681). This was supported by the Hoorn study (2004), a population based study that compared central artery stiffness in 261 subjects with normal glycemia, 170 subjects with IFG or IGT, and 188 subjects with type 2 DM. "In IGM [impaired glucose metabolism], values of central artery stiffness were intermediate between those of the groups with NGM [normal glucose metabolism] and

DM-2 [type 2 diabetes mellitus] (Schram et al., 2004, p. 179).

In the past ten years, the scientific research indicates that decreasing vascular compliance is independently associated with type 2 DM and, to a lesser degree, with both IGT and IGF. It is established that association occurs regardless of the presence of hypertension ($p = 0.01$ De Angelis et al., 2004; $p < 0.05$ Endemann et al. 2004). There is no evidence yet to determine if there is a difference between the sexes.

A limiting factor that must be considered when critiquing the literature related to vascular compliance and glucose status is the overall age of the populations researched. In some research it is possible that arterial stiffness was under-estimated in elderly populations studied due to selective mortality with diabetes. (Henry et al., 2003; van Dijk, Dekker, et al., 2001).

Although type 2 DM and its preceding IGT population make up the majority of the population with diabetes and glucose intolerance, special diabetic populations still need to be researched. It is important to assess whether the conclusions presented extend to women who have had a pregnancy complicated by GDM, whether the glucose levels returns to normal or not post delivery.

Gestational Diabetes

Insulin resistance

The majority of women with GDM appear to have pre-existing β cell dysfunction as well as insulin resistance (Buchanan, 2001; Homko, Sivan, Chen, Reece, & Boden, 2001). In normal pregnancy, marked insulin resistance develops in the second trimester and progresses throughout the remainder of the pregnancy. If there is already insulin resistance present prior to pregnancy, it causes an additional effect. This results in

women with GDM having greater insulin resistance than pregnant women with normal glucose tolerance.

An additional study has shown that even though women with GDM have β cell dysfunction that occurs on a background of chronic insulin resistance, they still respond to the escalating insulin resistance. "The increase occurs along an insulin sensitivity-secretion curve that is approximately 50% lower (i.e. 50% less insulin for any degree of insulin resistance) than that of normal women" (Buchanan & Xiang, 2005, p. 485).

Prevalence

The prevalence of GDM in a general population is population specific, reflecting the underlying incidence of DM in the country of origin and the nature of the indigenous population. Therefore, areas with a high concentration of a population at high risk for the development of DM, such as Aboriginal, Hispanic, South Asian, Asian or African decent, would have a correlated increased incidence of GDM. In Canada, the first prospective survey within a defined geographical area identified the incidence of GDM as "3.5% for women in the general population and 11.5% for aboriginal women" (Dyck, Klomp, Tan, Turnell, & Boctor, 2002, p. 487).

A known risk factor for GDM is obesity or a body mass index of ≥ 30 kg/m² (Canadian Diabetes Association, 2003). Results from the 2004 Canadian Community Health Survey, based on directly measured height and weight, indicate that 23% of adults were obese, up from 14% in 1978/79, and, in 2004, an additional 36% of Canadians were overweight (Tjepkema, 2004). Thus, the prevalence of GDM will continue to rise in Canada, reflective of the rise of obesity in the general population.

Vascular compliance

Endothelial dysfunction post GDM, was first identified by Anastasiou et al. (1998) in both obese and non-obese, healthy women three to six months postpartum with normal glucose tolerance and no hypertension. The assessment of endothelial function, by brachial flow-mediated dilation, and interestingly the endothelial dysfunction was similar in both groups of women with a history of GDM, regardless of weight.

Hu, Norman, Wallensteen, and Gennser (1998), also established abnormal vascular function at both the macrovascular and microvascular level in healthy women with a history of GDM when compared to a control group of women of similar age. The researchers concluded that 2-4 years after pregnancy complicated by GDM, these women had increased common carotid artery wall stiffness, as measured by ultrasound, as well as diminished vasodilator response to acetylcholine of the micro vessels of the hand and foot assessed by laser Doppler technique.

Vascular compliance has also been researched during pregnancy. Paradisi, Biaggi, Ferrazzani, Carolis, and Caruso (2002) evaluated endothelial function, along with carbohydrate and lipid metabolism, in a small population of non-hypertensive, non-smoking Caucasian women. Endothelial function in 10 women with IGT and 13 with GDM were compared to a control group of 15 subjects during the third trimester of pregnancy. All three groups were matched for age, parity, and gestational week of testing. The women with GDM had a significantly higher body mass index (BMI) compared to the control subjects. Ultrasound was used to measure brachial artery flow-mediated dilation (FDM) and FDM was significantly reduced for the IGT group ($p < 0.04$) and for the GDM group ($p < 0.0001$) when compared to the controls. The results of

this study were "1) compared with control pregnancies, women with abnormal carbohydrate metabolism show an impaired FMD, more remarkable in subjects with GDM than those with IGT; and 2) FMD is inversely and strongly related to glucose area" (p. 563). These findings were independent of lipid metabolism and BMI.

Hannemann, Liddel, Shore, Clark, and Tooke (2002) wanting to assess whether vascular dysfunction may predate the development of hyperglycemia, chose to research healthy, normoglycemic women with a history of GDM, matched with control subjects for BMI, age and smoking. There were no differences between the two groups for variables associated with vascular risk. This study concluded that maximum microvascular vasodilator capacity (MMVC) measured by laser Doppler technique on heated areas of the foot, was significantly reduced post GDM when compared to the control subjects ($p = 0.008$). However, there was no significant difference in brachial artery dilation, before and after sublingual nitro-glycerine, between the groups ($p = 0.48$).

Concerned that menstrual cycle phase may influence vascular function, Heitritter, Solomon, Mitchell, Skali-Ounis, and Seely (2005) controlled for menstrual cycle phase in measuring vascular dysfunction, in pre-menopausal, non-hypertensive, women taking no medication, one year postpartum with either a history of GDM or normal pregnancy. Brachial pulse-wave analysis was used to measure vessel stiffness. Women with a history of GDM had increased peripheral vascular resistance when compared to the control group ($p \leq 0.04$) when matched on menstrual cycle phase.

These limited studies indicate a reduction in vascular compliance may exist at both a macro-vascular and micro-vascular level in healthy women who have experienced a

pregnancy complicated by IGT or GDM. In addition, during pregnancy complicated by GDM, the reduced vascular compliance was inversely related to elevated glycemic levels, which is consistent with published data on vascular function in subjects with normal glucose tolerance, IFG, IGT, and DM.

Measurement of Vascular Compliance

Vascular compliance is a marker for vascular disease. In assessing the pathophysiological changes in blood vessels associated with cardiovascular events, Glasser et al. (1997) noted, "changes in the arterial wall leading to reductions in arterial compliance may precede the onset of clinically apparent disease and may identify individuals at risk before disease onset..." (p. 1175). Given this, an accurate, direct, non-invasive method is needed to recognize those at risk for CVD, providing earlier and cost-effective preventative therapy.

Waveform Analysis

Description. Pulse-wave analysis (PWA) is generated through a generalized transfer function through a computerized process, taken of the creation of arterial waveform by the ventricular contraction that is reflected from the peripheral branch points. "The transfer function between the ascending aorta and the radial artery is relatively constant in adult humans and is used to generate the aortic waveform from the pressure wave in the radial artery" (O'Rourke, 1999, p. 46).

As a measure of arterial stiffness at a generated pressure, the stiffer the vessel, the higher the velocity for the pressure wave to travel the length of the vessel, which if reflected in the increased amplitude of the wave, is referred to as the augmentation index (AIx) (Figure 2.1). "The augmentation index, which is the difference between the first

and second systolic peaks expressed as a percentage of pulse pressure, … [is] a measure of systemic stiffness" (Mackenzie, Wilkinson, & Cockcroft, 2002, p. 72).

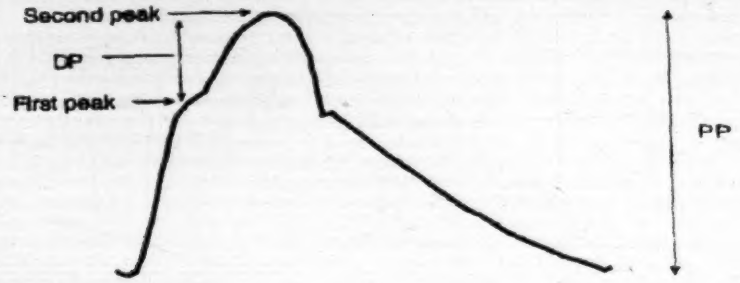


Figure 2.1

A typical central aortic pressure waveform in a middle aged subject. The second systolic peak becomes more prominent ... as arteries stiffen, as is caused by wave reflection. The augmentation index is defined at the difference between the second and first systolic peaks (ΔP) expressed as a percentage of the pulse pressure. (O'Rourke, 1999)

The method used to record PWA is applanation tonometry, an instrument used to measure pressure at the radial or carotid artery by establishing the force needed to flatten the artery. As a result of the soft tissue between the skin and the anterior wall of the artery, tonometry must be calculated. "The radial wave can be calibrated with reasonable precision from the brachial cuff sphygmomanometer" (Black et al., 1999, p. 9). As well, to maintain precision, a pressure transducer is located over the radial artery and secured by a strap, which automatically adjusts itself to detect the best waveform to reduce operator error.

Rationale for Use. Not only can a precise measurement be obtained using applanation tonometry, but the time required to do so is relatively small, comparative to the time to obtain an electrocardiogram. As well, waveform analysis has been proven to

be an accurate measurement for vascular compliance for both large vessels (Resnick et al., 2000) and small vessels (McVeigh et al., 1999), and is reproducible (Liang et al., 1998).

Applanation tonometry for PWA is a non-invasive measurement of vascular compliance that correlates well with endothelial dysfunction (Nigam, Mitchell, Lambert, & Tardif, 2003) and with an increased risk for CVD (Weber et al., 2004).

Waveform analysis, using tonometry, is less operator-dependent when compared to ultrasound. Ultrasound is dependent on the ability of the operator to image the wall of reproducible, non-invasive, operator independent tool, that measures conduit vessels stiffness, in a relatively short time, to assess endothelial dysfunction and the risk for the vessels accurately, and with limited resolution, which makes detection of small changes in vessel diameter difficult. Due to this, there have been concerns about the reproducibility of this technique (Mackenzie, Wilkinson, & Cockcroft, 2002).

Limitations. There are limitations with PWA that must be considered. Pulse wave velocity gradually increased with heart rate in elderly subjects as demonstrated in a study by Lantelme, Mestre, Lievre, Gressard, and Milon, 2002, and this higher velocity could be reflected in the AIx in the waveform analysis.

Certain medications have been identified that influence the AIx, such as vasoactive medication that alter vascular tone. AIx was lowered with nitroglycerine administration and raised with angiotension administration. (Kelly, Millasseau, Ritter, & Chowienczyk, 2001). Additionally, vasopressor medications that inhibit basal nitric oxide (NO) synthesis influence Aix. NG-mono-methyl-L-arginine (L-NMMA) and norepinepherine increased AIx, while dobutamine decreased AIx (Stewart, Millasseau,

Kearney, Ritter, & Chowienczyk, 2003).

Insulin has also been researched by Westerbacka, Wilkinson, Cockcroft, Utriainen, Vehkavaara, and Yki-Jarvinen (1999) in relation to insulin's effect on large blood vessels with the use of applanation tonometry, measuring aortic waveforms and AIx in healthy males. The study subjects, with a small population of nine, was administered a six hour infusion of saline on one occasion and a two hour sequential insulin infusion to create a normoglycemic hyperinsulinemic state on another occasion. The researchers were able to conclude that "augmentation index decreased significantly within 1 hour after administration of insulin ($P<0.001$) but not saline" (p.1118).

Summation. Waveform analysis using applanation tonometry, is an accurate, CVD. However, waveform analysis must be used in consideration to other factors that may alter the measurability of AIx.

CHAPTER 3

Research Method

The purpose of this study is to determine vascular compliance in women with either IGT or IFG or both, and normal glucose tolerance, with a recent history of GDM.

Design

A cross-sectional, comparative design was used to assess vascular compliance in women, ages 18-44, with both abnormal glucose tolerance and normal glucose tolerance and a recent history of GDM. Vascular compliance in this population was compared to women with normal glucose metabolism, who have had a recent pregnancy not complicated by GDM, since the variables being researched cannot be manipulated. Women were assigned to one of three groups, based on the independent variable:

1. Women with normal glucose tolerance post GDM.
2. Women with either IGT or IFG post GDM.
3. Women with a normal pregnancy, not complicated by GDM, to act as a control group.

Sample

For the purpose of this study, women were selected by a non-probability, purposive sampling method based, on the independent variable, in the Edmonton region. Additional inclusion criteria for each participant in the study included:

1. Women with normal glucose tolerance post GDM.
   - Age 18-45 years.
   - History of GDM in the past 3-24 months.
   - Fasting plasma glucose (isolated) of < 5.7 mmol/L and/or a random plasma

glucose < 7.8 mmol/L.

2. Women with IGT/IFG post GDM

   - Age 18-45 years.
   - History of GDM in past 3-24 months.
   - Fasting plasma glucose (isolated) of 6.1-6.9 mmol/L and/or random plasma glucose (isolated) of 7.8-11.0 mmol/L.

3. Women with a recent pregnancy not complicated by GDM.

   - Age 18-45 years.
   - History of normal pregnancy in past 3-24 months.
   - Fasting plasma glucose (isolated) of < 5.7 mmol/L and/or a random plasma glucose < 7.8 mmol/L.

The exclusion criteria for all three groups included:

- Existing hypertension.
- Existing cardiovascular disease
- History of pre-eclampsia.
- History of cardiovascular disease.
- Use of ACE-inhibitors, angiotensin receptor blockers, alpha blockers, calcium channel blockers, or nitroglycerine in the previous three months.
- Previous history or new onset of diabetes mellitus (non-gestational).
- Current pregnancy.
- Pregnancy in the past three months.

Sampling Method

The access to the sample was obtained in the following manner. Women with a

recent history of GDM, who had been seen by the primary investigator, were recruited from the Pregnancy Clinic at the Grey Nuns hospital. Based on the results of their glucose tolerance test post pregnancy, they were stratified into either normal glucose tolerance or impaired glucose tolerance. These women were then contacted via telephone, by a recruiter who was not affiliated with the study explaining the purpose of the study and the brief involvement required by the volunteers. If interested these women were offered the opportunity to participate in the research at an arranged date and time.

Participants for the study initially went to an outpatient clinic at the Grey Nuns Hospital to be seen by the co-investigator, who again explained the intention of the study. Participants were then given the opportunity to ask questions, and discuss any concerns. After this, the information sheet was provided to participants to read prior to an informed consent being obtained. If the inclusion and exclusion criteria were met, the questionnaire was completed, waist:hip ratio was measured, and the PWA for vascular compliance was performed.

However many participants who volunteered for the study often did not come for their scheduled appointments. When contacted by the recruiter, the potential subjects often cited the difficulties of going out with an infant, and if no additional children, the inconvenience and expense of parking at the hospital. Due to the poor participation, the method for obtaining the sample population was altered.

The initial contact was still initiated by the recruiter to explain the purpose and time commitment of the study. If interested, the women were then contacted by the co-investigator to answer any further questions, and a date and time for a home visit was

arranged. At the home visit, questions and concerns were addressed by the co-investigator before the participants were given the information sheet and the consent form to sign. If the inclusion and exclusion criteria were met and after the questionnaire was completed, PWA was preformed and waist:hip ratio measured.

Women with no history of GDM, acting as the control group, were recruited from New Mom groups and friends of women with a history of GDM who had participated in the study. These women were given a recruitment poster (Appendix A) with contact information for the co-investigator to give to the women who had been recently pregnant and who might be interested in participating in research. If the co-investigator was contacted by these women, the research was explained, and a home visit was arranged.

Ethical Considerations

Ethical approval (Appendix B) was obtained from the Health Research Ethics Board (Panel B), Capital Health. Support from Dr. Chik, Endocrinologist, and the Patient Care Manager of the Metabolic Clinic at the Grey Nuns Hospital, was obtained for the implementation of this study.

Several strategies were utilized to protect the rights of the study women. First the study was explained both verbally and in writing via an Information Sheet (Appendix C), and the women were given an opportunity to have any outstanding questions answered. Following this, a signed consent was obtained (Appendix D). The study subjects were informed about the purpose of the study, which their participation was voluntary, and that they could withdraw from the study with no consequences to their medical or nursing care.

There are no risks to the women for participating in this study. Confidentiality of the

women was maintained by coding the data collection forms. The participant's names, code numbers, and data are on separate sheets, and kept in a locked filing cabinet. Only study investigators have access to this data. The data will be stores for 7 years beyond the conclusion of the study. No identifying data will be used in the publication of the study results.

Sample Size

The sample size for each the three groups was estimated to be twenty for an expected large effect size, and an α of .05 to achieve a minimal power of .8 (Cohen, 1988). However, recruiting enough participants to power this study was not accomplished, due to confounding factors. Only 3.5% for women in the general population and 11.5% for aboriginal women experience a pregnancy complicated by gestational diabetes (Dyck et al., 2002) and the Grey Nuns site sees very few aboriginal pregnant women. The population to recruit participants was further decreased as woman with a history GDM often do not complete an OGTT post partum. In a retrospective study Rambaldini, Hanley, & Feig (2006), only 38.1% of women with a pregnancy complicated by GDM completed their follow-up OGTT. This finding was similar to those by Russell et al. (2006) in which only 45% of women returned post partum for the OGTT. Given the small percentage of women who have a pregnancy complicated by GDM, the less than 50% of those that return for OGTT post partum, and the small number of healthy, young people that volunteer for research studies without being financially compensated (van Gelderen et al., 1993; Bigorra & Banos, 1990); the estimated sample size needed to power the study could not be obtained in a timely manner. Therefore 18 subjects were recruited for each group. Since the sample size

obtained was small, it was important to have groups of equal size to ensure the data results were proportionate for each group.

Data Collection

All women were given an information sheet (Appendix C) of the study to read and have any question clarified, prior to the informed consent (Appendix D) being obtained by the co-investigator. A copy of the information sheet and consent was provided to all study subjects. If requested, the family physician would be informed of the subject's involvement in the study. Additionally, the women were given a questionnaire (Appendix E) to complete detailing their risk factors for cardiovascular disease and decreased arterial compliance. With the women's permission, patient charts were reviewed for medical history, to ensure these women met the inclusion and exclusion criteria (Appendix F) of the study.

Women who agreed to participate in the research and met both the inclusion and exclusion criteria, were seen either in the Outpatients Clinic at the Grey Nuns Hospital or in their home. The women with a history of GDM and healthy controls, who met both the inclusion and exclusion criteria, had non-invasive PWA performed using applanation tonometry with HDI/PulseWave™ Cardiovascular Profiling Instrument CR-2000 after they have been resting supine for five minutes in a quiet room, without smoking or caffeine consumption in the previous 30 minutes. The instrument was strapped to the arm, and blood pressure, systemic vascular resistance, large artery compliance, and small artery compliance was measured and recorded. Following this, a measurement of waist:hip ratio was obtained.

No medication or radiation was administered and no further testing was required.

Time commitment was estimated to be approximately 30 minutes, which included listening to a brief explanation of the purpose of the study, giving informed consent, completing a questionnaire, and participating in the study.

Operational Definitions

Vascular Compliance

An absolute term referring to the vascular elasticity and the storage of the vessels.

Pulse Wave Analysis (PWA)

The analysis of arterial stiffness using an instrument to generate arterial waveform from ventricular contractions that are reflected from the pressure wave in the radial artery. As a measure of arterial stiffness at a generated pressure, the stiffer the vessel, the higher the velocity for the pressure wave to travel the length of the vessel, which is reflected in the increased amplitude of the wave.

Applanation tonometry

A method used to record PWA.

HDI/PulseWave ™Cardiovascular Profiling Instrument CR-2000

An instrument that provides a sensitive, non-invasive way to measure the changes in the elasticity of both small and large arteries (http://www.apc-cardiovascular.co.uk/cr2000.htm). To illustrate, an example is provided (Figure 3.1).

Data Analysis

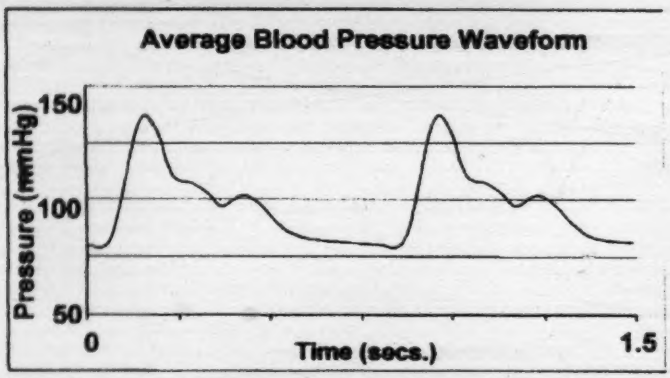
Data analysis was performed using SPSS (Version 15) was used for one way analysis of variance (ANOVA) to test for differences in vascular compliance, blood pressures, waist:hip ratio, and ethnicity. The final data was expressed as a F value, with $P < 0.05$ being statistically significant. A regression analysis was completed to assess the

effect of age on vascular compliance.

Research CardioVascular Profile Report

Research Subject ID:
Protocol 1743
Research Subject Name:
DOE, JOHN M

Date: 23 SEPT 1999
Time: 14:35
Age: 34 years
Gender: Male
Height: 71 in
Weight: 189 lbs.
BSArea: 2.06 sq. meters
Body Mass Index: 26.4



PARAMETER	RESEARCH SUBJECT VALUE
SYSTOLIC BLOOD PRESSURE (mmHg)	136
DIASTOLIC BLOOD PRESSURE (mmHg)	79
MEAN ARTERIAL BLOOD PRESSURE (mmHg)	102
PULSE PRESSURE (mmHg)	57
PULSE RATE (beats/min)	72
ESTIMATED CARDIAC EJECTION TIME (msec)	293
ESTIMATED STROKE VOLUME (ml/beat)	87
ESTIMATED STROKE VOLUME INDEX (ml/beat/m^2)	42
ESTIMATED CARDIAC OUTPUT (L/min)	6.3
ESTIMATED CARDIAC INDEX (L/min/m^2)	3.1
LARGE ARTERY ELASTICITY INDEX (ml/mmHg x 10) (Capacitive Arterial Compliance)	14.9
SMALL ARTERY ELASTICITY INDEX (ml/mmHg x 100) (Oscillatory or Reflective Arterial Compliance)	11.1
SYSTEMIC VASCULAR RESISTANCE (dyne•sec•cm^{-5})	1226
TOTAL VASCULAR IMPEDANCE (dyne•sec•cm^{-5})	111

Figure 3.1

Sample of a HDI/PulseWave ™CR-2000 Profile Report

CHAPTER 4

Results

The purpose of this chapter is to present the results of the research. The characteristics of the participants will be described, followed by a presentation of the findings relative to differences in vascular compliance, blood pressures, waist:hip ratio in women with a history of GDM as compared to a control group. The effect of glucose tolerance on vascular compliance will also be compared. In addition, the impact of ethnicity and age on vascular compliance and blood pressure will be reported.

Participant Characteristics

From September 2006 to January 2007, a total of 54 women participated in this study. These participants represented a purposeful sampling of women with a recent history of pregnancy. Eighteen women were assigned to each of the three groups based on the independent variables; impaired glucose tolerance (IGT) post GDM, normal glucose tolerance (NGT) post GDM, and a control group. All participants completed the questionnaire to determine clinical characteristics of this sample. The mean age of the IGT group was 36 with an age range of 30 to 41, the NGT group mean age was 33 with an age range of 28 to 44, and the control group mean age was 30 with an age range of 18 to 42. The waist:hip ratios were higher in women with a history of GDM compared to the control group. Of note, there was an equal number of Caucasian, East Indian, and Chinese women in the IGT population, compared to the NGT and control groups whose majority were Caucasian. In addition, the IGT group consisted of 17 women who had never smoked compared with the NGT groups with only 8 subjects who had never smoked and 10 of the control group who had never smoked. Activity hours between the

groups were comparable with the control group being the most active with 5 women doing more than 21 hours of activity a week. As expected, the women with a history of GDM had a larger proportion of family members with a history of diabetes. There was a slight increase of family members with a history of vascular disease for the IGT group compared with both the other groups. There was no notable difference in medications taken between the three groups of women. Table 1 describes the clinical characteristics of this sample.

Glucose Tolerance on Vascular Compliance, Blood Pressure, and Waist:Hip Ratio

Measurements of vascular compliance of the large and small arteries, blood pressure, and waist:hip ratio were obtained. One way ANOVA with a $p < 0.05$ was used to test for differences. Diastolic blood pressure was significant at a $p = 0.015$ and waist:hip ratio was significant with a $p < 0.001$. Figures 4.1- 4.5 depicts the outcomes between the IGT post GDM group, the NGT post GDM group, and the control group. Both groups of women with a history of GDM demonstrate a higher waist:hip ratio than the controls (Figure 4.5).

Table 1

Participants Demographics and Clinical Characteristics

Demographics & Characteristics	IGT post GDM (n=18)	NGT post GDM (n=18)	Control (n=18)
Age (Mean ± SEM)	36±3	33±4	30±2
Waist:Hip Ratio (Mean ± SEM)	0.93±0.02	0.94±0.21	0.79±0.01
Ethnicity			
Caucasian	5 (28%)	11 (61%)	14 (78%)
Filipino	2 (11%)	3 (17%)	1 (6%)
	5 (28%)	1 (6%)	0
Chinese	5 (28%)	3 (17%)	1 (6%)
Other	1 (6%)	0	2 (11%)
Smoking			
Current	0	4 (22%)	(22%)
Quit	1 (6%)	6 (33%)	4 (22%)
Never	17 (94%)	8 (44%)	10 (56%)
Activity Hours			
< 7 hours/week	10 (56%)	15 (83%)	10 (56%)
7-21 hours/week	6 (33%)	2 (11%)	3 (17%)
> 21 hours/week	2 (11%)	1 (6%)	5 (28%)
Family History of Diabetes			
Yes	8 (44%)	9 (50%)	(22%)
No	10 (56%)	8 (44%)	14 (78%)
Unknown	0	1 (6%)	0
Family History of Vascular Disease			
Yes	6 (33%)	4 (22%)	4 (22%)
No	12 (67%)	13 (72%)	13 (72%)
Unknown	0	1 (6%)	1 (6%)

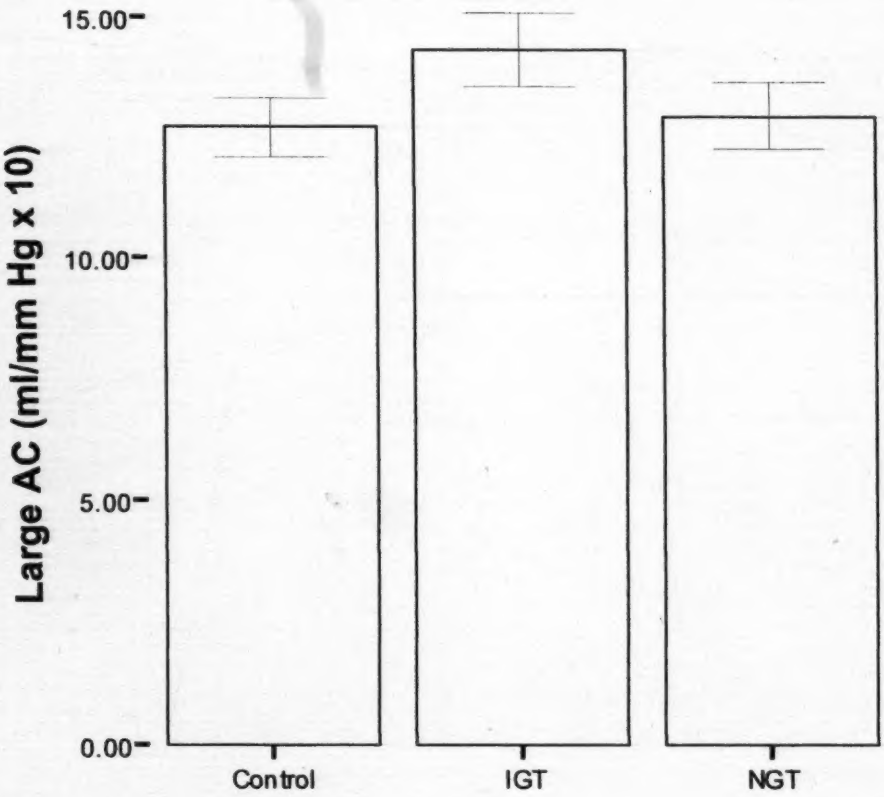


Figure 4.1

Graph of Difference of Large Artery Compliance (AC) between Groups

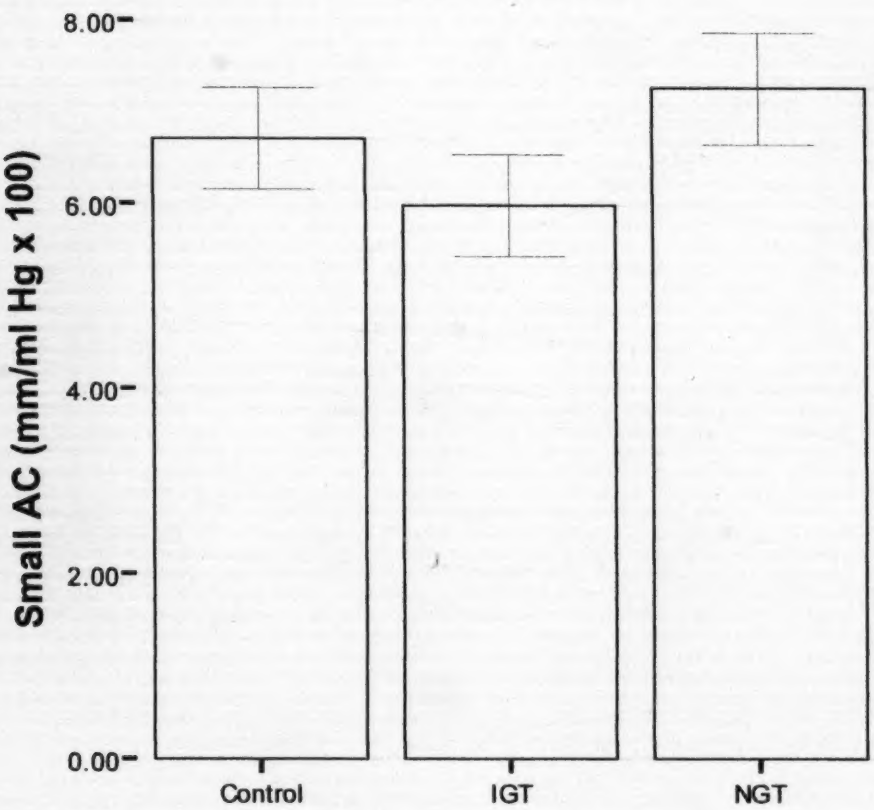


Figure 4.2

Graph of Differences of Small Artery Compliance (AC) between Groups

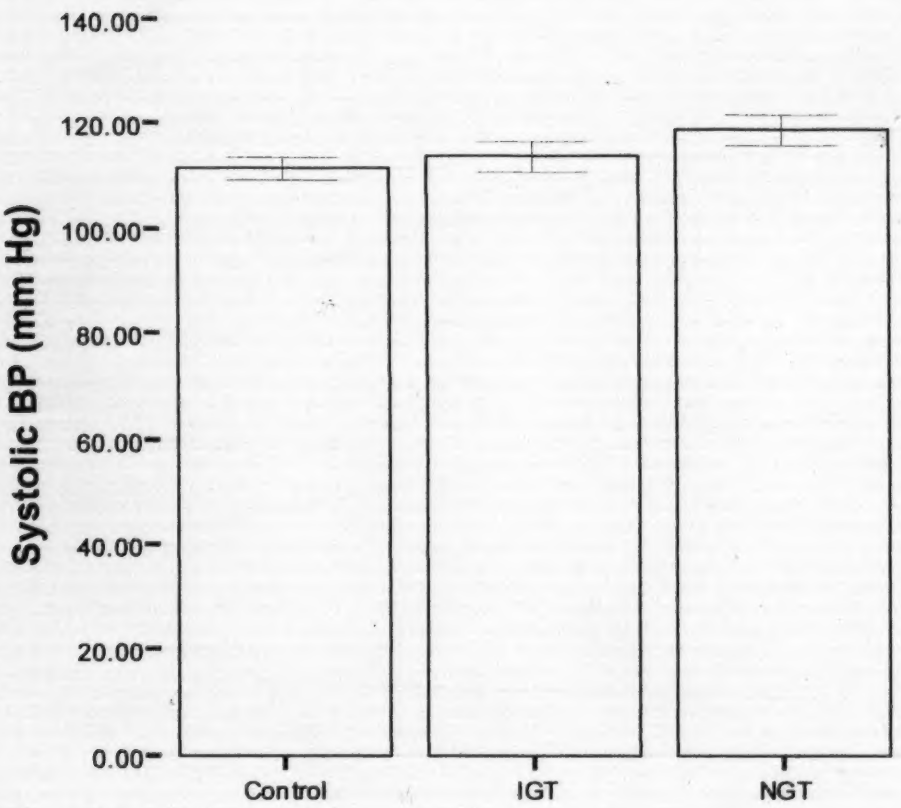
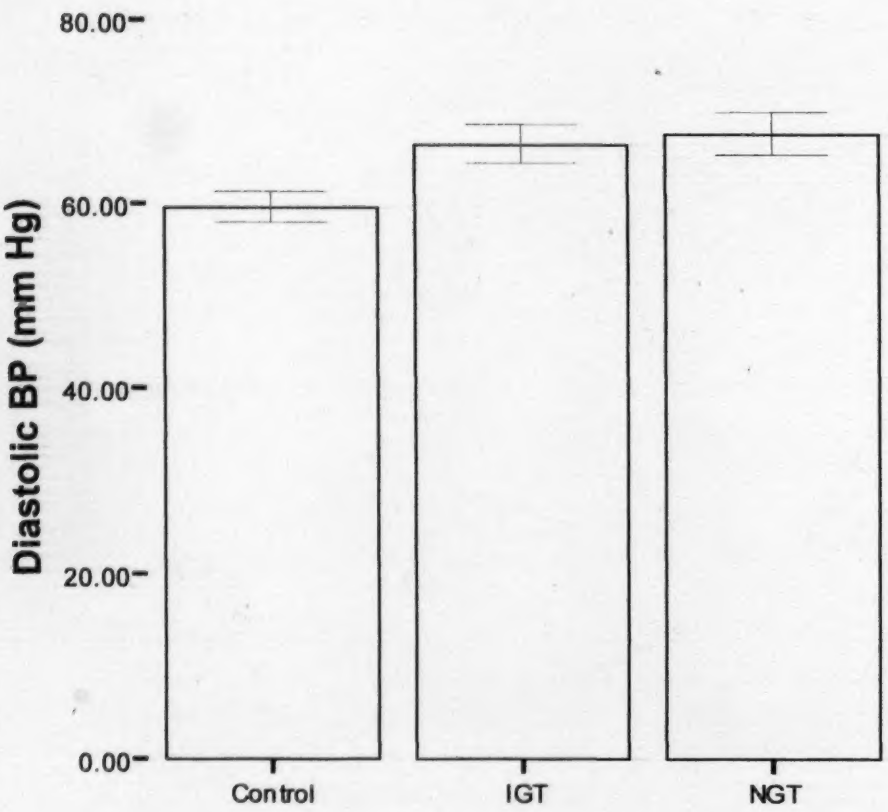


Figure 4.3

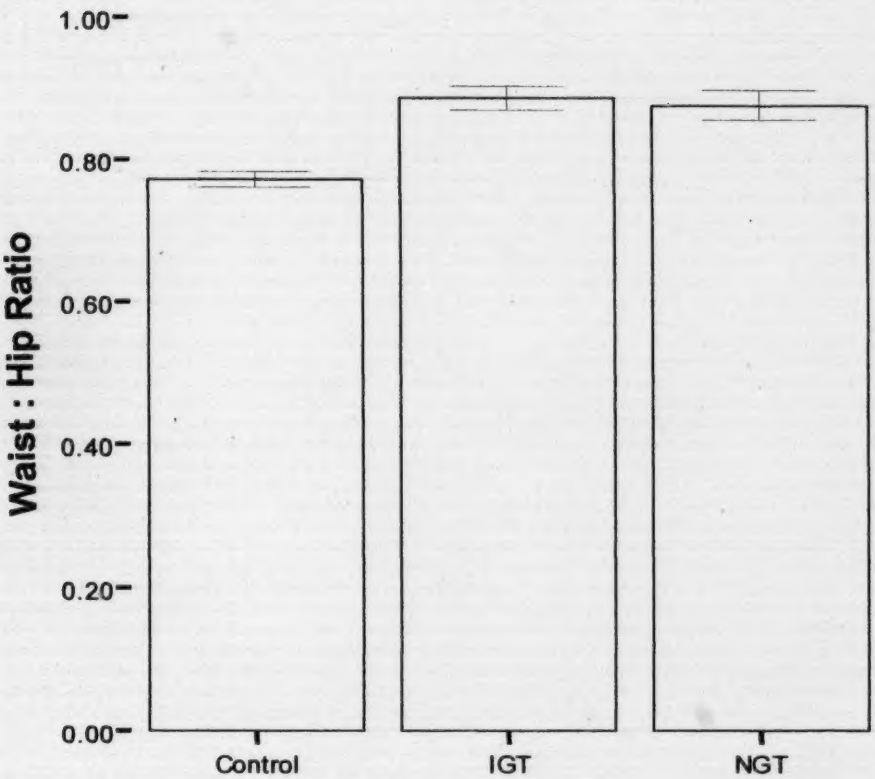
Graph of Differences of Systolic Blood Pressure (BP) between Groups



*p = 0.015

Figure 4.4

Graph of Differences of Diastolic Blood Pressure (BP) between Groups



*p < 0.001

Figure 4.5

Graph of Differences of Waist:Hip Ratio between Groups

As there were only significant differences on two of the dependent variables, none being vascular compliance, further post hoc testing was completed. The two groups of women with normal glucose tolerance post pregnancy were combined into one larger group (n = 36). The vascular compliance of the large and small arteries, and the systolic and diastolic blood pressure for these groups was compared to the smaller group of women (n = 18) with glucose intolerance post pregnancy. All results (Table 2), including diastolic blood pressure, were insignificant ($p < 0.05$).

Table 2

One Way ANOVA between the group with impaired glucose tolerance (n =18) and the combined group of normal glucose tolerance (n = 36)

Source	*Mean ± SEM*		*F*	*p*
	IGT	*NGT*		
Large Artery Compliance	14.33 ± 0.77	12.84 ± 0.46	3.180	0.080
Small Artery Compliance	6.99 ± 0.41	5.98 ± 0.56	2.087	0.155
Systolic Blood Pressure	113.72 ± 2.81	115.14 ± 1.89	0.181	0.673
Diastolic Blood Pressure	66.44 ± 2.17	63.53 ± 1.54	1.202	0.278

Note: $p < 0.05$

Ethnicity and Age on Vascular Compliance, Blood Pressure, and Waist to Hip Ratio

Further analysis was done to identify if there were any differences in vascular compliance and blood pressure in the 3 groups based on ethnicity and/or age. Some of the ethnic populations had only one participant, therefore ethnic origin was grouped for non-Caucasian and Caucasian only and vascular compliance and blood pressure

measured. No significant differences were seen between the two groups (Table 3).

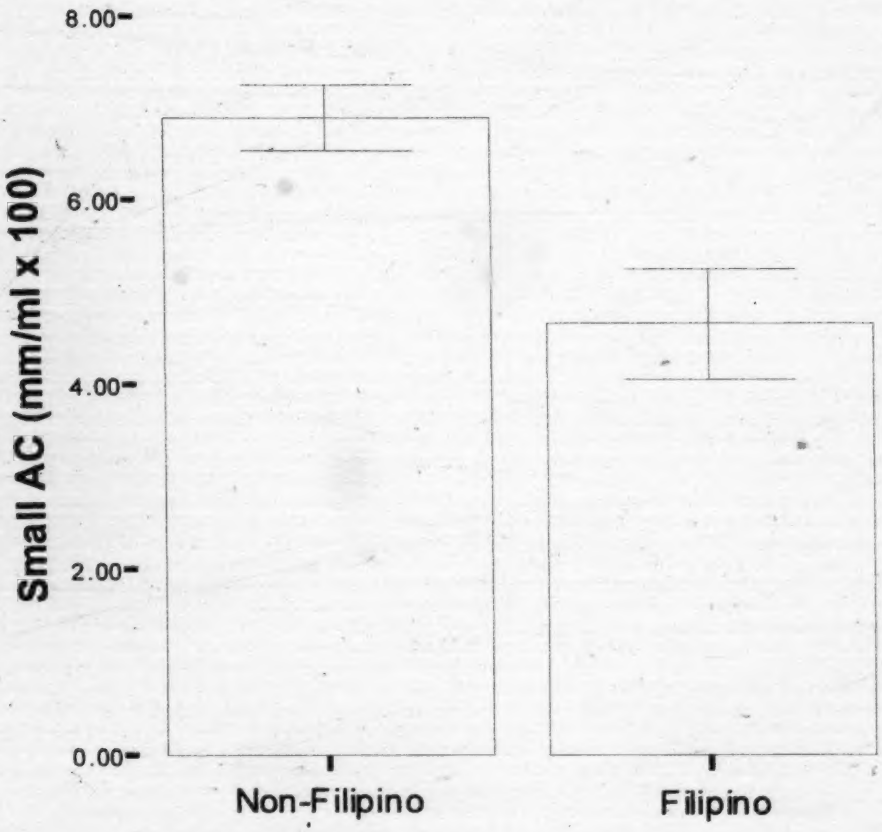
Table 3

One way ANOVA comparing Vascular Compliance and Blood Pressure in Caucasians (N=29) and Non-Caucasians (N=25)

Source	*Mean ± SEM*		*F*	*p*
	Caucasians	*Non-Caucasians*		
Large Artery Compliance	12.98 ± 0.47	13.77 ± 0.70	0.911	0.344
Small Artery Compliance	6.48 ± 0.35	6.87 ± 0.62	0.341	0.562
Systolic Blood Pressure	117.37 ± 1.89	111.29 ± 2.47	3.956	0.052
Diastolic Blood Pressure	5.03 ± 1.72	63.83 ± 1.87	0.222	0.640

Note: $p < 0.05$

When the raw data was viewed, it appeared that overall the Filipino population had reduced compliance in their small arteries; therefore, additional one way ANOVA was used to test for differences in vascular compliance. Although the population was small ($n = 6$), there was a significant difference ($p = 0.034$) for the small artery compliance. The differences between the groups are shown in Figure 4.6.

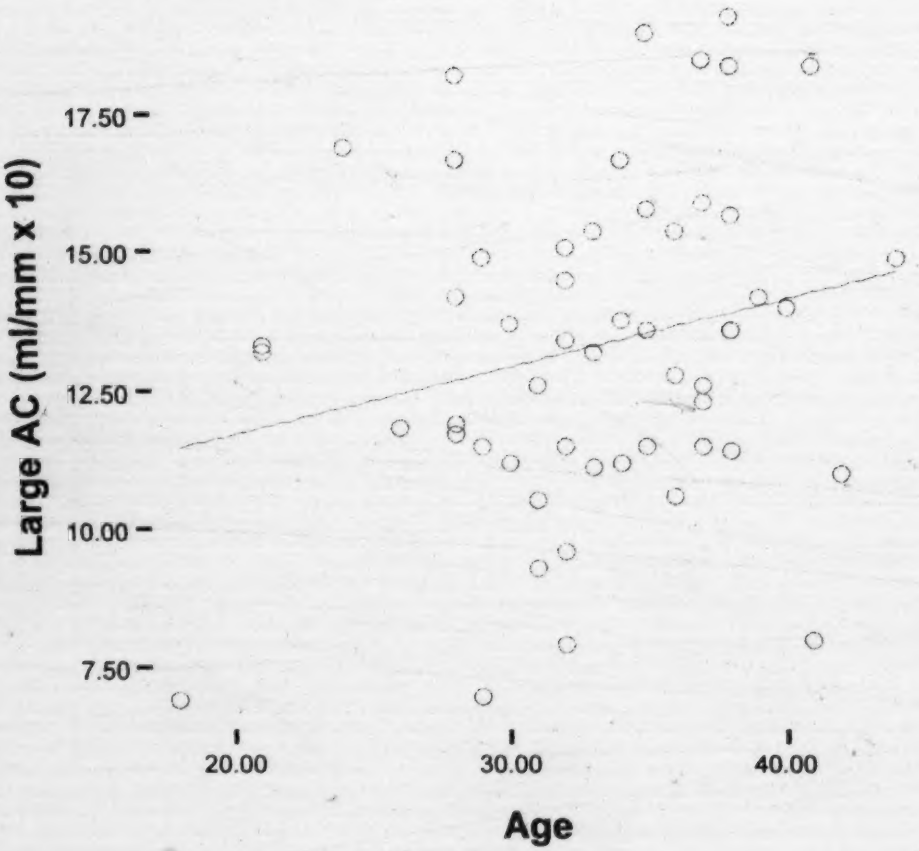


p = 0.034, Non-Filipino n = 48, Filipino n = 6

Figure 4.6

Differences of Small Artery Compliance between Filipinos and Non-Filipinos

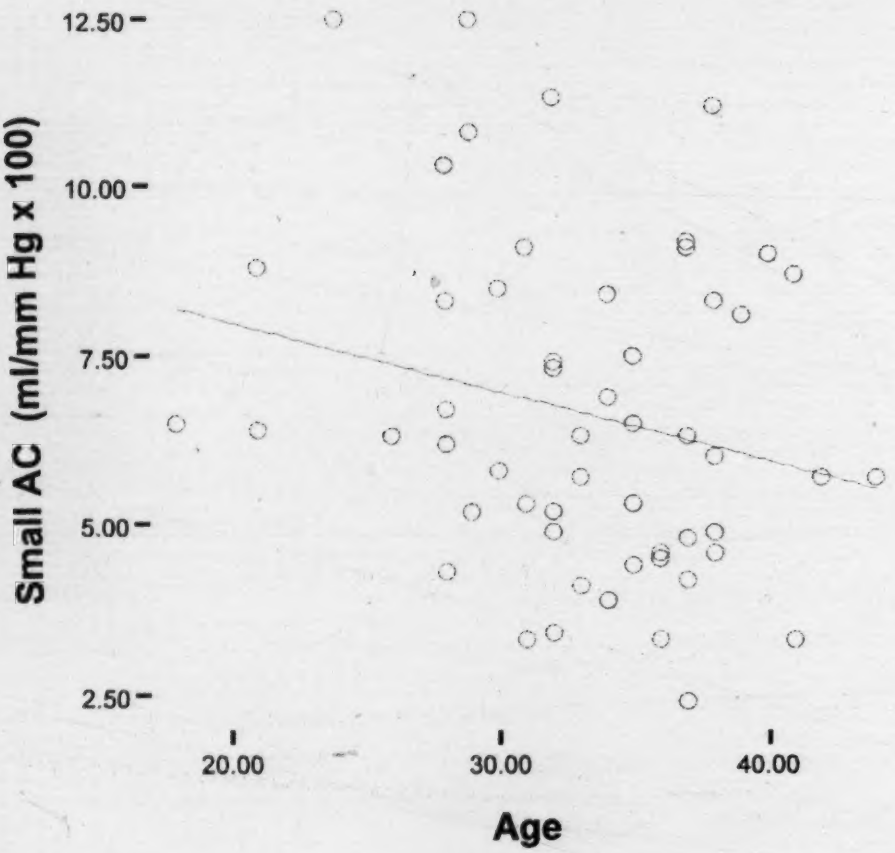
Finally, because there was a notable age difference between the three groups being studied further statistical analysis was completed assessing the effect of age on large and small artery compliance, furthermore this was noted as a limiting factor for some of the research in the literature review. The results were not significant for this study for large arteries ($p = 0.107$) (Figure 4.7) and for small arteries ($p=0.104$) (Figure 4.8).



Note: $R^2 = 0.05$

Figure 4.7

Regression Analysis of Age to Large Artery Compliance



Note: $R^2 = 0.05$

Figure 4.8

Regression Analysis of Age to Small Artery Compliance

Chapter 5

Discussion

In chapter 5 the discussion of the research findings in relation to the literature is presented. The significant finding of this study was that waist:hip ratio is related to glucose intolerance with pregnancy. As well, there is evidence suggesting that there could be an association between Filipinos and diminished small artery compliance. Surprisingly, no correlation was discovered between glucose tolerance and vascular compliance in women with a history of GDM in this limited study. These findings are presented with implications for nursing practice, along with limitations, strengths, and direction for further research.

Relationship of Waist:Hip Ratio to Glucose Tolerance and CVD

Waist to hip ratio was significantly higher in women with a history of GDM, irrespective of glucose status post pregnancy. It is postulated that the majority of these women were over weight pre-pregnancy with an increased abdominal girth, as weight gain and inactivity cause insulin resistance. Türkoglu et al. (2003) concluded that insulin resistance increases as abdominal fat increases. In reviewing the relationship between insulin resistance and endothelial dysfunction, Yki-Jarvinen (2003) found that in vivo "insulin … appears to markedly potentiate endothelium-dependent vasodilatation. Therefore, anything that impairs insulin action in endothelial cells can be expected to be associated with endothelial dysfunction" (p. 411). Long before individuals with insulin resistance develop abnormal glucose intolerance, pro-atherogenic changes occur but the underlying mechanisms remain poorly understood (Semenkovic, 2006). In 2005 the Prospective Pioglitazone Clinical Trial in Macrovascular Events (PROACTIVE) was

completed, comparing insulin sensitizing oral medication to a placebo in 5,238 patients with type 2 diabetes and known vascular disease. Overall, there were 177 deaths with the insulin sensitizing medication that reduced insulin resistance and 186 with placebo (Dormandy et al., 2005).

Ethnicity and Vascular Compliance

Small artery compliance was significantly reduced in the Filipino subjects when compared to the rest of the combined ethnic population in the study. Although, only 11% of the small study population was Filipino and it was not the primary investigation, the significance of the result warrants further examination.

Only a small number of studies have investigated the risk of cardiovascular disease for Filipinos and no research has been done in regards to their vascular compliance. Ryan et al. (2000) completed a four year study on cardiac outcomes post percutaneous coronary intervention or cardiac surgical treatment comparing Filipinos or Filipino-Americans to Caucasians. These researchers found that Filipino-Americans have a higher incidence of hypertension and diabetes compared to Caucasians, as well as a higher mortality rate following cardiac catheterization ($p < 0.001$). Another cross sectional investigation was done by Colin Bell, Adair, & Popkin (2002) into the relationship of hypertension and BMI for ethnicity with adults aged 30-65 from China ($n = 3423$), the Philippines ($n = 1929$) and the United States ($n = 7957$). Filipino women had a higher incidence of hypertension at every level of BMI compared with non-Hispanic Whites and Mexican Americans.

Adair (2004) followed Filipino women over a 16 year period to estimate the risk of hypertension associated with overweight, obesity, and high waist-to-hip ratio. With a

high waist to hip ratio of 0.85, there was a 2.5 fold increase in risk of developing a systolic blood pressure of ≥ 160 or a diastolic blood pressure of ≥ 100.

From the previous studies, it would seem more likely that Filipinos are at an increased risk of cardiovascular disease when compared to Caucasians, especially Filipino women as they have an overall higher incidence of hypertension. However recent research has been done comparing Filipinos and Caucasian women with no known cardiovascular disease. By measuring a marker of atherosclerotic plaque Araneta & Barrett-Connor (2004) establish no significant difference between the Filipino (9-13%) and Caucasian (9-11%) women. Clearly more research is required in this area.

Vascular Compliance, Glucose Tolerance & Pregnancy

There was no correlation of decreased vascular compliance to glucose status in women with a history of GDM. This held even when women who were still glucose intolerant post pregnancy were compared to all women with normal glucose tolerance. This finding was unexpected given the strong literature supporting a decrease in vascular compliance with increasing glucose intolerance.

The literature was reviewed for vascular compliance in women during and post pregnancy with only very limited results. In a very small study ($n = 110$ for each group) van der Heijden et al. (2005) compared pregnant rats to non-pregnant rats and discovered that the gene expression of a long effect vasodilator (adrenomedullin) was increased during the first half of the rats pregnancy ($p < 0.05$). The researchers concluded that "this coincides and may be functionally related to the institution of a high flow/low resistance circulation in pregnancy" (p. 35). Research into the effects of adrenomedullin on women during pregnancy was completed but only in relation to blood volume. Adrenomedullin

levels were compared to a control group and women at 15-18 weeks gestation, as well as at full term. Results were significant ($p = 0.0009$) with increasing levels of adrenomedullin in the blood plasma during pregnancy (Hayashi et al., 2005).

Clapp 3rd. and Capeless (1997) studied cardiovascular functioning in healthy nulliparous ($n = 15$) and parous ($n = 15$) women. Baseline measurements of heart rate, arterial pressure, left ventricular volumes, cardiac output, and calculated peripheral resistance were obtained pre pregnancy. These measurements were repeated every 8 weeks during pregnancy and 12, 24, and 52 weeks postpartum. Cardiac output and decrease in peripheral resistance were significantly greater after pregnancy, especially in the parous women. Although postpartum values gradually returned towards baseline they did remain considerably higher from pre-pregnancy values in women who both breast fed and were physically active. It is possible that the existing decreased vascular resistance one year post delivery could counteract changes secondary to glucose intolerance in our study since the majority of the subjects were studied within one year of delivery.

The previous evidence suggests that pregnancy might have a cardio-protective effect for women, but if so, for how long? One subject in the control group had verbalized that she and a female friend, had participated in another study on vascular compliance 5.5 years previously, before pregnancy. These women were contacted by the recruiter, and they were informed of the results of this study, and that the researchers were interested in comparing results of their vascular compliance before and after pregnancy. These women were seen by the co-investigator and copies of their previous vascular compliance, measured using an HDI/PulseWave™ Cardiovascular Profiling Instrument

CR-2000, were obtained. The woman, who had not previously participated in this study, was then seen at the Clinical Investigation Unit at the University of Alberta hospital. She gave an informed consent and completed the questionnaire after reading the information sheet. Both women were healthy, non-smokers, taking no medication, with no history of diabetes. Pre-pregnancy and post pregnancy results were compared. In one of the subjects, S.L., the large artery compliance was improved from 12.1 to 15.8 with the small artery compliance slightly decreasing from 7.4 to 6.5, eighteen months post pregnancy. However, this was not consistent for the other subject. J. R. had a decrease in both large compliance from 20.5 to 13.8 and small artery compliance from 7.2 to 4.7 four years after her last pregnancy. These examples indicate that pregnancy may improve large artery compliance within 18 months of pregnancy, but this benefit may not be maintained with time, but are these results reproducible? Further studies definitely need to be completed to assess whether pregnancy is cardio-protective.

Implications for Nursing Practice

In today's health care system, nurses' roles are constantly changing and expanding, and their scope of practice is evolving. This is related to the overall change to primary health care for disease prevention and health promotion, which has been endorsed by the Canadian Nurses Association (2002) as the most effective way of providing health care to a population.

Nurses whether working in the community, or at a hospital, are in contact with overweight and obese individuals everyday. This may not be the primary reason the individual is being seen, but that does not mean that this risk for type 2 diabetes and cardiovascular disease should be ignored until the individual has overt symptoms of

these diseases. Health promotion and disease prevention can be initiated and followed by nurses in a variety of setting.

The relatively new, developing role of the advanced nurse practitioner (ANP) in Canada provides the nurse with the advanced knowledge and skills to provide quality health care in a variety of settings. The nurse practitioner has advanced education and experience in an area of clinical specialization to provide care. Although the ANP is grounded in knowledge that is derived from nursing theory, practice is extended into other traditional health care roles and as such, nurse practitioner needs to complete research that contributes to this aspect of the nursing professions body of knowledge. "In advanced nursing practice, the nurse makes use of scientific theories drawn from nursing and other disciplines, as well as current research, which enable her/him to articulate the reason for selecting nursing actions" (Canadian Nurses Association, 1997, p. 2).

Therefore, until the mechanisms underlying the relationship of cardiovascular disease to insulin resistance are better understood, the optimal treatment for reducing cardiac risk in individuals who have an increased waist to hip ratio is not medication but the promotion of a healthy lifestyle to reduce abdominal obesity. This can even prevent the development of type 2 diabetes. The Diabetes Prevention Program (2002) reported a 58% reduction in the incidence of diabetes over almost 3 years in subjects treated with a lifestyle intervention program of weight loss and physical activity. Hamman et al. (2006) estimates that individuals at risk of developing diabetes could even further reduce their diabetes risk by greater than 90% by losing more that 5-7% body weight and meeting their dietary and physical activity goals.

Lipscombe and Hux (2007) reported that the incidence of diabetes increased 69% in

the past 10 years in Ontario, Canada due to the increased prevalence and declining mortality caused by the disease. Given the astounding increased incidence of diabetes, effective nursing measures should definitely be implemented to prevent diabetes from developing.

Advanced Nurse Practitioners are providing expert care to individuals in a variety of settings. In their scope of practice, the ANP is going to encounter women from a variety of ethnicities with abdominal obesity and a history of pregnancy or plans to become pregnant. It is often the nurse practitioner that does the initial assessment and spends the most time with individuals and their families. This provides the opportunity to educate individuals and their families and promote health and well being based on scientific knowledge.

If Filipinos are at higher risk of developing cardiovascular disease than other ethnic groups, nurses need to use this knowledge to aggressively promote the health and well being of this population, to prevent the development of hypertension and type 2 diabetes, diseases which often precede the development of cardiovascular disease.

To quote Hildegard Peplau in an address to the June, 1997 International Congress of Nursing meeting in Vancouver, British Columbia, Canada "The key question that dominated the 20th century was: What do nurses do? In the next century the key question will become: What do nurses know and how do they use that knowledge to benefit people?"

Strengths, Limitations, and Direction for Future Research

The quality of a study and its findings are determined by how the investigator has addressed the issues of reliability and validity within the study. Reliability is concerned

with the accuracy (consistency, stability, and repeatability) of a measure in representing the true score of the participant being assess on a particular dimension" (Buckwalter, Mass, & Wakefield, 1998, p.47).

Strengths

A key strength of this study was the instrument used to measure vascular compliance. Using a comparative design it is essential that the instrument used to measure vascular compliance is accurate. The HDI/PulseWave™ Cardiovascular Profiling Instrument CR-2000 provides a sensitive, non-invasive way to measure vascular compliance and its proprietary, patented arterial waveform analysis methodology is fast, reliable, and easy to use (www.apc-cardiovascular.co.uk/cr2000.htm). Using this method and instrument for data collection ensured reliability of this research.

Although PWA is a recognized and proven method to determine vascular compliance it has been shown to be influenced by medications that alter vascular tone. Therefore it was imperative to include vasoactive medications in the exclusion criteria to control for this. In addition, pre-eclampsia can alter vascular tone. "Findings indicate that the decreased vasodilatation response in pre-eclamptic women is probably related to endothelial dysfunction" (Yoshida, Nakao, Kobayashi, & Kobayashi , 2000, p. 403). Consequently, a history of pre-eclampsia was also included in the exclusion criteria to enhance reliability in this study.

Limitations

Validity entails that the data being generated is actually representative of the variables being studied. Ideally, to control for this, subjects between the groups would

be matched on all perceived variable that could affect vascular compliance. Not only should the women be assigned to groups based on glucose levels post GDM, with a results compared to a control group of women with normal glucose tolerance after a uncomplicated pregnancy, but to establish internal validity, subjects should also be matched for age and cardiac risk factors including smoking, waist:hip ratio, and blood pressure. However, given the sample size needed, the relatively small population of GDM to draw from, and the limited time for data collection, this was not possible. This is a limitation of the research.

There were significant differences between the women with the history of GDM and the control group. Notably, the control group was younger and thinner than the treatment group, but when age was analysed there was no significant difference between the groups in its association with vascular compliance. In addition, the majority of the IGT post GDM group had never smoked with only one subject who had quit smoking, compared to the control with 4 current smokers and 5 ex-smokers.

The major limitation of this study was the sample size. There were not enough subjects in each group to reach a power of 0.05 to prevent the occurrence of a type 2 error, and it was estimated that the treatment effect would have a large impact on the outcome.

Future Research

Cardiovascular disease is a major health concern for Canadians, especially those living with diabetes. It is known that increasing glucose intolerance is associated with decreasing vascular compliance, yet this was not the result of this study. Since decreased vascular compliance is a risk for CAD, this study should be repeated with a larger

sample size, taking into consideration confounding variables including age, waist:hip ratio, ethnicity, smoking history, activity levels, and family history of diabetes and cardiovascular disease. It would also be of interest to investigate whether pregnancy is cardio-protective by measuring vascular compliance pre and post pregnancy in a longitudinal study to assess whether there was a benefit and how long this benefit could last for. Finally, more research needs to be completed on ethnic populations. It should be established whether certain ethnic populations, such as Filipinos are at greater risk than Caucasians for vascular disease. It is also important to establish evidence based practice behind nursing care. For example, in assessing cardiac risk the Framingham score does not take ethnicity into consideration, and this may need to be added in the future.

Conclusion

There is an established body of knowledge regarding the relationship of hyperglycemia to decreased vascular compliance in type 2 DM, and its predecessor of IGT. This is significant as decreased vascular compliance causes CVD. Of all the complications of diabetes, CVD has the highest mortality and morbidity, as well as economic burden.

GDM is a specific classification of DM, which consists of a small population of women who develop glucose intolerance in pregnancy. Only limited data exist that determine vascular changes in women with a history of GDM.

A cross-sectional, comparative design was used to assess vascular compliance, blood pressure, and waist:hip ratio in women with both abnormal glucose tolerance and normal glucose tolerance with a recent history of GDM, compared to a healthy control group. Vascular compliance was assessed using applanation tonometry with

HDI/PulseWave™ Cardiovascular Profiling Instrument CR-2000, a sensitive, reliable, non-invasive method to measure and record changes in the compliance of both small and large arteries. The data generated was analyzed using SPSS software with a one way analysis of variance (ANOVA) to test for differences in vascular compliance, blood pressure, and waist:hip ratio between the groups of women. Regression analysis was implemented to assess the effect of age on vascular compliance.

The research did not detect changes in vascular compliance in women with a recent history of GDM compared to a control group. This result was maintained even when all the women were classified as IGT or NGT and vascular compliance was compared. This could be related to the decreased vascular resistance that occurs during pregnancy that persists for at least one year post partum.

The significant findings of this research is that a woman's waist:hip ratio is related to glucose tolerance and that the Filipino women have significantly less compliant small arteries than the rest of the research population. This is important for the delivery of nursing care especially in the environment of primary health care. Nurses will encounter women with abdominal obesity whether they work in a teaching facility, a managerial position, or are the front line workers in the community or hospital setting. These women will be at risk for the development of type 2 diabetes and its major complication of CVD, more so if they have other risk factors such as hypertension, smoking, or family history of diabetes or CVD. It is essential that all risk factors for both type 2 diabetes and CVD are addressed early to prevent the development of these devastating diseases.

Furthermore, if the women in this study did not have decreased vascular compliance related to the protectiveness of pregnancy, this has to be researched. Women with GDM

are heavier than their counter parts and as such are already at risk for cardiovascular disease. If these women will develop further reduction in the vascular compliance in the near future, they need to know, so that every measure can be taken into account for the delivery of care to prevent the development of the cardiovascular disease.

Nursing has the rationale needed to implement nursing care plans focusing on the modifiable risk factors to promote the health and well being of these women. If implemented it would result in the reduction of type 2 diabetes and the incidence of both CVD mortality and morbidity of this population.

References

Adair, L. S. (2004). Dramatic rise in overweight and obesity in adult filipino women and risk of hypertension. *Obesity Research, 12*(8), 1335-1341.

Anastasiou, E., Lekakis, J. P., Alevizaki, M., Papamichal, C. M., Megas, J., Souvatzoglou, A., et al. (1998). Impaired endothelium dependent vasodilatation in women with previous gestational diabetes. *Diabetes Care, 21*(12), 2111-2115.

Araneta, M. R. & Barrett-Connor, E. (2004). Subclinical coronary atherosclerosis in asymptomatic Filipino and white women. *Circulation, 110*(18):2817-2823.

Bigorra, J. & Banos, J. E. (1990). Weight of financial reward in the decision by medical students and experienced healthy volunteers to participate in clinical trials. *European Journal of Clinical Pharmacology. 38*(5):443-6.

Black, H. R., Kuller, L. H., O'Rourke, M. F., Weber, M. A., Alderman, M. H., Benetos, A., et al. (1999). The first report of the Systolic and Pulse Pressure (SYPP) Working Group. *Journal of Hypertension, 17*(Suppl. 5), 3-14.

Buchanan, T. A. (2001). Pancreatic B-cell defects in gestational diabetes: implications for the pathogenesis and prevention of type 2 diabetes. *Journal of Clinical Endocrinology & Metabolism, 86*(3), 989-93.

Buchanan, T. A., & Xiang, A. H. (2005). Gestational diabetes mellitus. *The Journal of Clinical Investigation, 115*(3), 485-491.

Buckwalter, K. C., Mass, M. L., & Wakefield, B. (1998). Classical experimental designs. In P. J. Brink & M. J. Wood (Eds.), *Advanced design in nursing research,* (2nd ed.). Thousand Oaks, CA: SAGE Publications, Inc.

Canadian Diabetes Association (2003). Clinical practice guidelines for the prevention

and management of diabetes in Canada. *Canadian Journal of Diabetes, 27*(Suppl 2).

Canadian Nurses Association (1997). Out in front: Advanced nursing practice. *Nursing Now: Issues and Trends in Canadian Nursing, 2,* 1-4.

Canadian Nurses Association (2002). Fact sheet: Effective health care equal primary health care (PHC). *Publications & Resources.* Retrieved March 2, 2007 from http://www.cna-nurses.ca/CNA/documents/pdf/publications/FS17 _Effective_ Health_Care_Equals_Primary_Health_Care_Nov_2002_e.pdf

Canadian Nurses Association (2007). Advanced Nursing Practice. *Canadian Nurse Practitioner Initiative*. Retrieved January 20, 2007 from http://www.cnanurses.ca /CNA/practice/advanced/initiative/default_e.aspx

Clapp, J.F. 3rd. & Capeless, E. (1997). Cardiovascular function before, during, and after the first and subsequent pregnancies. *American Journal of Cardiology, 80*(11), 1469-1473.

Cohen, J. (1988). *Statistical power for the behavioural sciences.* Hillsdale, NJ: Lawrence Erlbaum.

Colin Bell, A., Adair, L. S. & Popkin, B. M. (2002). Ethnic differences in the association between body mass index and hypertension. *American Journal of Epidemiology, 155*(4), 346-353.

Coutinho, M., Gerstein, H. C., Wang, Y., & Yusef, S. (1999). The relationship between glucose and incident cardiovascular events. *Diabetes Care, 22*(2), 233-240.

De Angelis, L., Millasseau, S. C., Smith, A., Viberti, G., Jones, R. H., Ritter, J. M., et al. (2004). Sex differences in age-related stiffening of the aorta in subjects with type 2 diabetes. *Hypertension, 44*(1), 67-71.

Diabetes Prevention Program Research Group. (2002). Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *New England Journal of Medicine, 346*, 393–403.

Dormandy, J. A., Charbonnel, B., Eckland, D. J., Erdmann, E., Massi-Benedetti, M., Moules, I. K. et al. (2005). Secondary prevention of macrovascular events in patients with type 2 diabetes in the PROactive Study (PROspective pioglitAzone Clinical Trial In macroVascular Events): a randomised controlled trial. *Lancet, 366,* 1279–1289.

Dyck, R., Klomp, H., Tan, L. K., Turnell, R. W., & Boctor, M. A. (2002). A comparison of rates, risk factors, and outcomes of gestational diabetes between aboriginal and non-aboriginal women in the Saskatoon health district. *Diabetes Care, 25*(3), 487-493.

Emoto, M., Nishizawa, Y., Kawagishi, T., Maekawa, K., Hiura, Y., Kanda, H., et al. (1998). Stiffness indexes β of the common carotid and femoral arteries are associated with insulin resistance in NIDDM. *Diabetes Care, 21*(7), 1178-1182.

Endemann D. H., Pu, Q., De Ciuceis, C., Savoia, C., Virdis, A., Neves, M. F. et al. (2004). Persistent remodelling of resistance arteries in type 2 diabetic patients on antihypertensive treatment. *Hypertension, 43*(2), 399-404.

Folsom, A. R., Szklo, M., Stevens, J., Liao, F., Smith, R., & Eckfeidt, J. H. (1997). A prospective study of coronary heart disease in relation to fasting insulin, glucose, and diabetes. *Diabetes Care, 20*(6), 935-942.

Glasser, S. P., Arnett, D. K., McVeigh, G. E., Finkelstein, S. M., Bank, A. J., Morgan, D. J. et al. (1997). Vascular compliance and cardiovascular disease: a risk factor or a

marker? *American Journal of Hypertension, 10,* 1175-1189.

Grandinetti, A., Chang, H. K., Theriault, A., & Mor, J. (2005). Metabolic syndrome in a multiethnic population in rural Hawaii. *Ethnicity & Disease, 15*(2):233-237.

Haffner, S. M., Lehto, S., Ronnemaa, T., Pyorala, K., & Laakso, M. (1998). Mortality from coronary heart disease in subjects with type 2 diabetes and in no diabetic subjects with and without prior myocardial infarction. *The New England Journal of Medicine, 339*(4), 229-234.

Hamman, R. F., Wing, R. R., Edelstein, S. L., Lachin, J. M., Bray, G. A., Delahanty, et al. (2006). Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care. 29*(9), 2102-2107.

Hannemann, M. M., Liddell, W. G., Shore, A. C., Clark, P. M., & Tooke, J. E. (2002). Vascular function in women with previous gestational diabetes mellitus. *Journal of Vascular Research, 39,* 311-319.

Hayashi, Y., Ueyama, H., Mashimo, T., Kangawa, K., & Minamino N. (2005). Circulating mature adrenomedullin is related to blood volume in full-term pregnancy. *Anesthesia & Analgesia. 101*(6), 1816-1820.

Heitritter, S. M., Solomon, C. G., Mitchell, G. F., Skali-Ounis, N., & Seely, E. W. (2005). Subclinical inflammation and vascular dysfunction in women with previous gestational diabetes mellitus. *Journal of Clinical Endocrinology & Metabolis, 90*(7), 3983-3988.

Homko C., Sivan E., Chen X., Reece E. A. & Boden, G. (2001). Insulin secretion during and after pregnancy in patients with gestational diabetes mellitus. *Journal of Clinical Endocrinology & Metabolism. 86*(2), 568-73.

Hemodynamic monitoring HDI/PulseWave™ Cardiovascular Profiling Instrument CR-2000 (n.d.). Retrieved February 22, 2006 from http://www.apc-cardiovascular.co.uk/cr2000.htm

Henry, R. M. A., Kostense, P. J., Spijkerman, A. M. W., Dekker, J. M., Nijpels, G., Heine, R. J. et al. (2003). Arterial stiffness increases with deteriorating glucose tolerance status: The Hoorn Study. *Circulation, 107,* 2089-2095.

Hu, J., Norman, M., Wallensteen, M., & Gennser, G. (1998). Increased large arterial stiffness and impaired acetylchline induced skin vasodilatation in women with previous gestational diabetes mellitus. *British Journal of Obstetrics and Gynaecology, 105,* 1279-1287.

Kannal, W. B., & McGee, D.L. (1979). Diabetes and cardiovascular disease: The Framingham Study. *Journal of American Medical Association, 241,* 2035-2038.

Kelly, R. P., Millasseau, S. C., Ritter, J. M., & Chowienczyk, P. J. (2001). Vasoactive drugs influence aortic augmentation index independently of pulse-wave velocity in healthy men. *Hypertension, 37,* 1429-1433.

Kim, C., Newton, K. M., & Knopp R.H. (2005). Gestational diabetes and the incidence of type 2 diabetes: A systematic review. *Diabetes Care, 25,* 1862-1868.

Lantelme, P., Mestre, C., Lievre, M., Gressard, A., & Milon, H. (2002). Heart rate: an important confounder of pulse wave velocity assessment, *Hypertension, 39,* 1083-1087.

Liang, Y. L., Teede, H., Kotsopoulos, D., Shiel, L., Cameron, J. D., Dart, A. M., et al. (1998). Non-invasive measurements of arterial structure and function: repeatability, interrelationships and trial sample size. *Clinical Science, 95,* 669-679.

Lipscombe, L. L. & Hux, J. E. (2007). Trends in diabetes prevalence, incidence, and mortality in Ontario, Canada 1995–2005: a population-based study. *Lancet, 369,* 750-756.

Mackenzie, I. S., Wilkinson, I. B., & Cockcroft, H. J. R. (2002). Assessment of arterial stiffness in clinical practice. *QJM, 95,* 67-74.

McVeigh, G. E., Bratteli, C. W., Morgan, D. J., Alinder, C. M., Glasser, S. P., Kinkelstein, S. M., et al. (1999). Age-related abnormalities in arterial compliance identified by pressure pulse contour analysis: age and arterial compliance. *Hypertension, 33,* 1392-1398.

Metzger, B. E., & Coustan, D. R. (1998). Summary and recommendations of the fourth international workshop-conference of gestational diabetes mellitus. *Diabetes Care, 21*(Suppl. 2), B161-B167.

Moss, S. E., Klein, R., Klein, B. E. K., & Meuer, S. M. (1994). The association of glycaemia and cause-specific mortality in a diabetic population. *Archives of Internal Medicine, 154,* 2473-2479.

Nigam, A., Mitchell, G. F., Lambert, J., & Tardif, J. C. (2003). Relation between conduit vessel stiffness (assessed by tonometry) and endothelial function (assessed by flow-mediated dilation) in patients with and without coronary heart disease. *American Journal of Cardiology, 92,* 395-399.

O'Rourke, M.F. (1995). Mechanical principles in arterial disease. *Hypertension, 26*(1), 2-9.

O'Rourke, M.F. (1999). Wave travel and reflection in the arterial system. *Journal of Hypertension, 17*(Suppl. 5), 45-47.

Paradisi, G., Biaggi, A., Ferrazzani, S., De Carolis, S., & Caruso, A. (2002). Abnormal carbohydrate metabolism during pregnancy: association with endothelial dysfunction. *Diabetes Care, 25*(3), 560-564.

Rambaldini, G., Hanley, R., & Feig, D. S. (2006, October). *Adherence to postpartum oral glucose tolerance testing in women with gestational diabetes mellitus.* Poster session presented at the annual meeting of the Canadian Diabetes Association Canadian Society of Endocrinology and Metabolism Professional Conference and Annual Meetings, Toronto, ON

Resnick, L. M., Militianu, D., Cunnings, A. J., Pipe, J. G., Evelhoch, J. L., Soulen, R. L., et al. (2000). Pulse waveform analysis of arterial compliance: relation to other techniques, age and metabolic variables. *American Journal of Hypertension, 3,* 1243-1249.

Romney, J. S., & Lewanczuk, R. Z. (2001). Vascular compliance is reduced in the early stages of type 1 diabetes. *Diabetes Care, 24*(12), 2102-2106.

Russell, M. A., Phipps, M. G., Olson, C. L., Welch, H. G., & Carpenter, M.W. (2006). Rates of postpartum glucose testing after gestational diabetes mellitus. *Obstetrics & Gynecology. 108*(6), 1456-62.

Ryan, C., Shaw, R., Pliam, M., Zapolanski, A. J. Murphy, M., Valle H. V. et al. Coronary heart disease in Filipino and Filipino-American patients: prevalence of risk factors and outcomes of treatment. *Journal of Invasive Cardiology, 12*(3), 134-139.

Salomaa, V., Riley, W., Kark, J. D., Nardo, C., & Folsom, A. R. (1995). Arterial disease/hypertension/angiotensin system: Non-insulin-dependent diabetes mellitus

and fasting glucose and insulin concentrations are associated with arterial stiffness indexes: The ARIC study. *Circulation, 91*(5), 1432-1443.

Schram, M. T., Henry, R. M. A., van Dyjk, R. A. J. M., Kostense, P. J., Dekker, J. M., Nijpels, G., et al. (2004). Increased central artery stiffness in impaired glucose metabolism and type 2 diabetes: The Hoorn Study, *Hypertension, 43,* 176-181.

Semenkovich, C. F. (2006). Insulin resistance and atherosclerosis. *Journal of Clinical Investigation, 116*(7), 1813-1822.

Stamler, J., Vaccaro, O., Neaton, J. D., & Wentworth, D. (1993). Diabetes, other risk factors, and 12-yr cardiovascular mortality for men screened in the Multiple Risk Factor Intervention Trial. *Diabetes Care,16*(2), 434-444.

Stewart, A. D., Millasseau, S. C., Kearney, M. T., Ritter, J. M., & Chowienczyk, P. J. (2003). Effects of inhibition of basal nitric oxide synthesis on carotid-femoral pulse wave velocity and augmentation index in humans. *Hypertension, 42,* 915-918.

Tjepkema, M. (2004). Adult obesity in Canada: Measured height and weight. *Nutrition: Findings from the Canadian Community Health Survey.* Ottawa, ON: Statistics Canada. Available at http://www.statcan.ca/english/research/82-620-MIE/2005001/pdf/aobesity.pdf. Accessed February 19, 2006.

Turkoglu, C., Duman, B. S., Gunay, D., Cagatay, P., Ozcan, R. & Buyukdevrim, A. S. (2003). Effect of abdominal obesity on insulin resistance and the components of the metabolic syndrome: evidence supporting obesity as the central feature. *Obesity Surgery, 13*(5), 699-705.

van Dijk, R.A. J. M., Nijpels, G., Twisk, J. W. R., Steyn, M., Dekker, J. M., Heine, R. J., et al. (2000). Change in common carotid artery diameter, dispensability and

compliance in subjects with a recent history of impaired glucose tolerance: a 3-year follow-up study. *Journal of Hypertension, 18*(3), 293-300.

van der Heijden, O. W., Essers, Y. P., van Eyndhoven, H. W., Spaanderman, M. E., Aardenburg, R., van Eys G. J., et al. (2005). Vascular expression of adrenomedullin is increased in Wistar rats during early pregnancy. *European Journal of Obstetrics, Gynecology, & Reproductive Biology. 123*(1), 35-40.

UI: 16260338

van Dijk, R. A. J. M., Dekker, J. M., Nijpels, G., Heine, R. J., Bouter, L. M., & Stehouwer, C. D. A. (2001). Brachial artery pulse pressure and common carotid artery diameter: mutually independent associations with mortality in subjects with a recent history of impaired glucose tolerance. *European Journal of Clinical Investigation, 31,* 756-763.

van Gelderen, C. E., Savelkoul, T. J., van Dokkum, W., & Meulenbelt, J. (1993). Motives and perception of healthy volunteers who participate in experiments. *European Journal of Clinical Pharmacology. 45*(1):15-21.

Weber, T., Auer, J., O'Rourke, M.F., Kvas, E., Lassnig, E., Berent R., et al. (2004). Arterial stiffness, wave reflections, and the risk of coronary artery disease. *Circulation, 109,* 184-189.

Weinberger, M. H., Fineberg, N. S., & Fineberg, S. E. (2002). The influence of blood pressure and carbohydrate tolerance on vascular compliance in humans. *American Journal of Hypertension, 15*(8), 678-682.

Westerbacka, J., Wilkinson, I., Cockcroft, J., Utriainen, T., Vehkavaara, S., & Yki-Jarvinen, H. (1999). Diminished wave reflection in the aorta: a novel physiological action of insulin on large blood vessels. *Hypertension, 33,* 1118-1122.

Yki-Jarvinen, H. (2003). Insulin resistance and endothelial dysfunction. *Best Practice & Research Clinical Endocrinology & Metabolism, 17*(3):411-430.

Yoshida, A., Nakao, S., Kobayashi, M., & Kobayashi, H. (2000). Flow-mediated vasodilation and plasma fibronectin levels in preeclampsia. *Hypertension, 36*(3), 400-404

Appendices

Appendix A: Recruitment Poster

Appendix B: Ethical approval

Appendix C: Information Sheet

Appendix D: Consent Form

Appendix E: Questionnaire

Appendix F: Enrolment Criteria

Appendix A

Department of *Endocrinology and Metabolism*
University of Alberta

PARTICIPANTS NEEDED FOR RESEARCH ON BLOOD VESSEL STIFFNESS AFTER PREGNANCY

If you have been pregnant in the last two years and you may be eligible to take part in a research study. We are recruiting women who have had diabetes during their pregnancy, and those who did not.

As a participant in this study you would be asked to

- fill out an anonymous questionnaire
- have the stiffness of your blood vessels measured
- have your height and weight taken and your waist and hips measured

Your participation would involve one session, which would take approximately 20-30 minutes.

For more information about this study, or to volunteer for this study, please contact:

Cheryl Caul RN Research Nurse
telephone: 780-819-4729 or
e-mail: ccaul@shaw.ca

Appendix B

Health Research Ethics Board

2J3 Heritage Medical Research Centre
University of Alberta, Edmonton, Alberta, T6G 2S2
p: 780 492 9724 Biomedical Panel
p: 780 492 0368 Health Panel
p: 780 492 0459
p: 780 492 0839
f: 780 492 7800

ETHICS APPROVAL FORM

Date: September 2006

Name(s) of Principal Investigator(s): Dr. Constance Chik

Department: Medicine

Title: Noninvasive assessment of vascular compliance in patients with impaired fasting glucose and impaired glucose tolerance

The Health Research Ethics Board (Biomedical Panel) has reviewed the protocol involved in this project which has been found to be acceptable within the limitations of human experimentation. The REB has also reviewed and approved the patient information material and consent form.

Specific Comments:

D. W. Morrish, M.D., PhD
Chairman, Health Research Ethics Board
Biomedical Panel

This approval is valid for one year

Issue: **#4265**

UNIVERSITY OF ALBERTA

Capital Health

CARITAS HEALTH GROUP

Appendix C

INFORMATION SHEET

Assessment of Vascular Compliance in Women Post Gestational Diabetes with Impaired Fasting Glucose or Impaired Glucose Tolerance and Normal Glucose Tolerance

Principal Investigator: Dr. C. Chik

Co-investigator: Cheryl Caul RN, MN (Candidate)

Background: The number of people with type 2 diabetes mellitus (adult onset) is rising. This is a problem as diabetes increases the risk for problems such as heart attacks, stokes, kidney disease, eye disease, and nerve damage. As well, there are many people who do not use sugar properly and are at risk of getting diabetes. This is found on blood tests either after not eating or drinking all night (impaired fasting glucose) or after drinking a sugar liquid and testing the blood (impaired glucose tolerance). People at this stage may never develop full-blown diabetes, especially if they exercise and eat right. We do not know much about whether these people have higher risk of heart attacks and strokes. We do know that people with diabetes have arteries that are stiffer and less stretchy than people that do not have diabetes. This is important for their chances of having heart attacks and strokes. We do not know if women who have had diabetes during pregnancy have early changes of stiff arteries. If they do, we may need to think about earlier treatment and ways to live healthier to prevent heart attacks and strokes.

Purpose: You are being asked to participate in a research study to help us learn if people with high fasting glucose or impaired glucose tolerance have early stiffening of the arteries. You may be a woman with a history of diabetes during pregnancy, who does not have diabetes now, that may or may not use sugar properly. Or you may be a healthy person who never had diabetes during pregnancy, to let us check our research.

Procedures: Participating in this study will involve:

1. Completion of a questionnaire.

2. Placement of a special painless machine on your arm that will briefly take your blood pressure and measure waveforms or stiffness in your blood vessels.

Possible Benefits: Through this study we may learn more about the risk for heart disease and strokes in women who have had diabetes during pregnancy. This information may help us make decisions in the future about when and how to start treating women who are at risk.

Possible Risks: There are no risks in taking part in this study.

Confidentiality: Your information from this study will be kept confidential. Any report published as a result of this study will not identify you by name. Your consent to participate in this study also includes consent for the researchers to review all your medical records as may be necessary for the purpose of the study. By signing the consent form, you give permission to the researchers to access any personally identifiable health information, which is under custody of other health care professionals and is considered necessary to carry out the research.

Voluntary Participation: You are free to withdraw from the research study at any time, and your continuing medical care will not be affected in any way. If the study is not done or if it is discontinued at any time, the quality of your medical care will not be affected. If any knowledge gained from this or any other study becomes available which could influence your decision to continue in the study, you will be promptly informed.

Contact Names and Telephone Numbers: If you have concerns about your rights as a study participant, you may contact the Patient Relations Office of the Capital Health Authority, at (780) 407-1040 or the Corporate Hospital Officer at the Caritas Health Group at (780) 450-7501. They have no affiliation with the study investigators.

Please contact Cheryl Caul Dr. Chik if you have any questions or concerns:

Cheryl Caul, RN	Telephone Number: (780)-819-4729
Dr. C. Chik, Endocrinologist:	Telephone Number: (780)-407-7421 Pager Number: (780)-407-8822

Appendix D

CONSENT FORM

Title of Project: Assessment of Vascular Compliance in Women Post Gestational Diabetes with Impaired Fasting Glucose or Impaired Glucose Tolerance and Normal Glucose Tolerance

Principal Investigator: Dr. C. Chik Phone Number: (780) 407-7421

Co-investigator: Cheryl Caul RN MN (Candidate) Phone Number: (780) 819-4729

To be completed by the research subject:

	YES	NO
Do you understand that you have been asked to be in a research study?	☐	☐
Have you read and received a copy of the attached Information Sheet?	☐	☐
Do you understand the benefits and risks involved in taking part in this research study?	☐	☐
Have you had an opportunity to ask questions and discuss this study?	☐	☐
Do you understand that you are free to withdraw from the study at any time, without having to give a reason and without affecting your future medical care?	☐	☐
Has the issue of confidentiality been explained to you, and do you understand who will have access to your medical records?	☐	☐
Do you want the investigator(s) to inform your family doctor that you are participating in this research study? If so, give his/her name: Dr._____	☐	☐

Who explained this study to you? _____

I agree to take part in this study: **YES** ☐ **NO** ☐

Signature of Research Subject: _____

(Printed Name) _____

Date:_____

Signature of Witness: _____

I believe that the person signing this form understands what is involved in the study and voluntarily agrees to participate.

Signature of Investigator or Designee _____

THE INFORMATION SHEET MUST BE ATTACHED TO THIS CONSENT FORM AND A COPY GIVEN TO THE RESEARCH SUBJECT

Appendix E

QUESTIONNAIRE

Assessment of Vascular Compliance in Women Post Gestational Diabetes with Impaired Fasting Glucose or Impaired Glucose Tolerance and Normal Glucose Tolerance

Please answer the following questions and circle the right answers

1. How old are you? _____ Birth date: _____
2. Are you pregnant? YES NO
3. Have you ever had diabetes during pregnancy? YES NO
4. Have you ever been told you have diabetes, or taken insulin or pills to control your blood sugars when you were not pregnant ? YES NO
5. Have you ever been told you have high blood pressure? YES NO
6. Have you ever been told you have high cholesterol? YES NO
7. Do you smoke? YES NO

   If yes, for how long? _____

   How many cigarettes a day? _____
8. Have you ever smoked in the past? YES NO

   If yes, when did you quit? _____

   How many years did you smoke? _____

   How many cigarettes a day? _____
9. Has a parent or brother or sister ever had a heart attack or stroke? YES NO

If yes, who and at what age?_____

_____

_____

10. Have you ever had a heart attack? YES NO

    If yes, how old were you? _____

11. Have you ever had heart bypass surgery? YES NO

    If yes, how old were you? _____

12. Have you ever had a stroke? YES NO

    If yes, how old were you? _____

13. Have you ever been told you have angina? YES NO

14. When exercising do you get tightness, heaviness, or

    an uncomfortable feeling in your chest? YES NO

15. How many hours of physical activity do

    you do a week? _____

    This includes walking, gardening, vacuuming and similar activity

16. How many alcoholic drinks do you have a week? _____

17. Are you taking blood pressure medication? YES NO

    If yes, which ones? _____

    _____

    _____

18. Have your parents or any of your brother or

    sisters been diagnosed with diabetes? YES NO

    UNKNOWN

If yes, which ones and at what age _____

_____

_____

19. What is your ethnic background? _____

20. Are you taking any medication? YES NO

If yes, which ones

_____

_____

_____

_____

May we contact your family doctor, if necessary, to check your recent blood sugar levels and important blood work, or to get important medical information (for example, names of blood pressure medication you cannot remember)? All medical information remains confidential and results from this study will not be presented in a way that you could be identified.

YES NO

Name of family doctor _____

Thank you for your valuable assistance with this study

Date _____

Your signature _____

Your name (please print) _____

Witness _____ Signature _____

Appendix F

ENROLLMENT CRITERIA

INCLUSION CRITERIA	**YES**	**NO**
1. Age 18-45 years	☐	☐
2. History of pregnancy in past 3-24 months. with one of the following:	☐	☐
☐ History of GDM with a fasting plasma glucose (isolated) of < 5.7 mmol/L and/or a random plasma glucose <7.8 mmol/L post delivery.		
☐ History of GDM with a fasting plasma glucose (isolated) of 6.1-6.9 mmol/L and/or random plasma glucose (isolated) of 7.8-11.0 mmol/L post delivery.		
☐ History of normal pregnancy with a fasting plasma glucose (isolated) of < 5.7 mmol/L and/or a random plasma glucose < 7.8 mmol/L post delivery.		
3. Able to provide informed consent	☐	☐
EXCLUSION CRITERIA		
1. Existing hypertension.	☐	☐
2. Existing cardio-vascular disease	☐	☐
3. History of pre-eclampsia.	☐	☐
4. Use of ACE-inhibitors, angiotensin receptor blockers, alpha blockers, calcium channel blockers, or nitroglycerine in the previous three months.	☐	☐
5. Previous history or new onset of diabetes mellitus (non-gestational).	☐	☐
6. Current pregnancy.	☐	☐
7. Pregnancy in the past three months.	☐	☐
8. History or cardiovascular disease.	☐	☐